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DATE: Thursday, September 11, 2003

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DB=USPT,PGPB,JPAB,EPAB,DWPI; PLUR=YES; OP=ADJ

L14	(17 or 18) near10 (depressi\$4 or antidepress\$6)	123	L14
L13	18 same 110	23	L13
L12	16 same 18	2	L12
L11	13 same 15	0	L11
L10	dissoc\$ or refract\$4 near3 depressi\$4	73732	L10
L9	11 same 13	0	L9
L8	nalmefene or naloxone or naltrexone or nalbuphine or thebaine or kappa agonist	3191	L8
L7	(opiate\$1 or opioid\$1) near3 antagonis\$4	1756	L7
L6	(depressi\$4 or antidepress\$4)near5 dissocia\$6	27	L6
L5	(depressi\$4 or antidepress\$4)near5 dissocia\$6	0	L5
L4	(depressi\$4 or antidepress\$4)near dissocia\$6	6	L4

DB=USPT,PGPB; PLUR=YES; OP=ADJ

L3	(depressi\$4 or antidepress\$4)near dissocia\$6	5	L3
L2	6080736.pn.	1	L2
L1	6132724.pn.	1	L1

END OF SEARCH HISTORY

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=> file medicine

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=> s depressi? or antideress? (s) dissociation
30 FILES SEARCHED...
L1 1204255 DEPRESSI? OR ANTIDERESS? (S) DISSOCIATION

=> s depressi? or antidepress?
L2 1388563 DEPRESSI? OR ANTIDEPRESS?

=> s dissocia?
L3 670508 DISSOCIA?

=> s l2 (s) l3
L4 3968 L2 (S) L3

=> s opiate? or opioid?

30 FILES SEARCHED...

L5 411408 OPIATE? OR OPIOID?

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L6 2578933 ANTAGONIS?

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=> s opiate? or opioid? (s) antagonis?

L7 233041 OPIATE? OR OPIOID? (S) ANTAGONIS?

=> d his

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EMBASE, ESBIODBASE, IFIPAT, IPA, JICST-EPLUS, KOSMET, LIFESCI, MEDICONF,
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2003

L1 1204255 S DEPRESSI? OR ANTIDERESS? (S) DISSOCIATION

L2 1388563 S DEPRESSI? OR ANTIDEPRESS?

L3 670508 S DISSOCIA?

L4 3968 S L2 (S) L3

L5 411408 S OPIATE? OR OPIOID?

L6 2578933 S ANTAGONIS?

L7 233041 S OPIATE? OR OPIOID? (S) ANTAGONIS?

=> s nalmeffene or naloxone or naltrexone or nalbuphine or thebaine

L8 186472 NALMEFENE OR NALOXONE OR NALTREXONE OR NALBUPHINE OR THEBAINE

=> s 14 and 17

L9 114 L4 AND L7

=> s amitriptyline or lofepramine or bupropion or citalopram or fluoxetine or fluvoxamine or
imipramine or paroxetine or sertraline or venlafaxine or nefazodone or nortriptyline or
mirtazapine or reboxetine or SAM-e

12 FILES SEARCHED...

28 FILES SEARCHED...

L10 253977 AMITRIPTYLINE OR LOFEPRAMINE OR BUPROPION OR CITALOPRAM OR FLUOX
ETINE OR FLUVOXAMINE OR IMIPRAMINE OR PAROXETINE OR SERTRALINE
OR VENLAFAXINE OR NEFAZODONE OR NORTRIPTYLINE OR MIRTAZAPINE OR
REBOXETINE OR SAM-E

=> s 19 and 110

L11 8 L9 AND L10

=> s 110 and 18

L12 4049 L10 AND L8

=> s 14 and 112

L13 13 L4 AND L12

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L14 12 DUP REM L13 (1 DUPLICATE REMOVED)

=> d l14 1-12 ibib, kwic

L14 ANSWER 1 OF 12 IFIPAT COPYRIGHT 2003 IFI on STN DUPLICATE 1
AN 10343482 IFIPAT;IFIUDB;IFICDB
TITLE: TREATMENT OF REFRACTORY DEPRESSION WITH AN OPIATE
ANTAGONIST AND AN ANTIDEPRESSANT
INVENTOR(S): Glover; Hillel, New York, NY, US
PATENT ASSIGNEE(S): Unassigned
AGENT: DICKSTEIN SHAPIRO MORIN & OSHINSKY LLP, 2101 L STREET
NW, WASHINGTON, DC, 20037-1526, US

	NUMBER	PK	DATE
PATENT INFORMATION:	US 2003087896	A1	20030508
APPLICATION INFORMATION:	US 2001-925190		20010809
FAMILY INFORMATION:	US 2003087896		20030508
DOCUMENT TYPE:	Utility		
	Patent Application - First Publication		
FILE SEGMENT:	CHEMICAL		
	APPLICATION		
NUMBER OF CLAIMS:	22		
AB	An antidepressant or a pharmaceutically acceptable salt thereof, and an opiate antagonist or a pharmaceutically acceptable salt thereof, are used to treat refractory depression characterized by dissociation .		
ECLM	1. A method for treating refractory depression characterized by dissociation , comprising administering to a patient in need thereof an effective dissociation reversing amount of an opiate antagonist or a pharmaceutically acceptable salt thereof; and an effective depression reversing amount of an antidepressant or a pharmaceutically acceptable salt thereof.		
ACLM	3. The method of claim 2, wherein the opiate antagonist is selected from the group consisting of nalmefene , naloxone , naltrexone , nalbuphine , thebaine , and combinations thereof.		
	6. The method of claim 1, wherein the effective dissociation reversing amount comprises an initial dosage of Nalmefene in the amount of about 50 mgs. b.i.d. for about three days, followed by a dosage of about 100 mgs.. . .		
	11. The method of claim 1, wherein the antidepressant is selected form the group consisting essentially of amitriptyline , lofepramine , bupropion , citalopram , fluoxetine , fluvoxamine , imipramine , paroxetine , sertraline , venlafaxine , nefazodone , nortriptyline , mirtazapine , reboxetine , SAM-E and combinations thereof.		
	12. The method of claim 1, wherein the effective depression reversing amount comprises an initial dosage of Bupropion SR in the amount of about 100 mgs. to about 300 mgs. one time daily.		
	13. The method of claim 1, wherein the effective depression reversing amount comprises a dosage of Venlafaxine in the amount of about 75 mgs. per day to about 375 mgs. one time daily.		
	14. A method for treating refractory depression characterized by dissociation comprising administering to a patient in need thereof an effective amount of (a) an antidepressant ; and (b) an opiate antagonist.		
	16. The method of claim 14, wherein the opiate antagonist is selected from the group consisting of nalmefene , naloxone , naltrexone , nalbuphine , thebaine , and combinations thereof.		
	18. The method of claim 14, wherein the antidepressant is selected form the group consisting essentially of amitriptyline , lofepramine , bupropion , citalopram ,		

fluoxetine, fluvoxamine, imipramine,
paroxetine, sertraline, venlafaxine,
nefazodone, nortriptyline, mirtazapine,
reboxetine, SAM-E and combinations thereof.

19. A method of treating refractory **depression** characterized by **dissociation** comprising administering to a patient in need thereof at least one opiate antagonist; evaluating said patient for a response to said opiate antagonist; reassessing said patient for **depression**; and administering at least one **antidepressant** to said patient.

L14 ANSWER 2 OF 12 USPATFULL on STN

ACCESSION NUMBER: 2003:195316 USPATFULL

TITLE: Electroencephalography based systems and methods for

selecting therapies and predicting outcomes

INVENTOR(S): Suffin, Stephen C., Sherman Oaks, CA, UNITED STATES

Emory, W. Hamlin, Malibu, CA, UNITED STATES

Brandt, Leonard J., San Juan Capistrano, CA, UNITED

STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003135128	A1	20030717
APPLICATION INFO.:	US 2002-193735	A1	20020711 (10)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 2000-501149, filed on 9 Feb 2000, PENDING Continuation-in-part of Ser. No. US 2001-930632, filed on 15 Aug 2001, PENDING		

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-304627P	20010711 (60)
	US 2001-304628P	20010711 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	PENNIE AND EDMONDS, 1155 AVENUE OF THE AMERICAS, NEW YORK, NY, 100362711	
NUMBER OF CLAIMS:	62	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	15 Drawing Page(s)	
LINE COUNT:	4945	

DETD . . . the familiar therapeutic entities PROZAC 435 and EFFEXOR 440. Similarly, Class 2 410 include MAOI 445 and Class 3 includes **Bupropion** 450.

DETD . . . (with as many as 7% of users being even slower metabolizers, i.e., having even longer half-lives for the active ingredient **fluoxetine** hydrochloride), and (2) it is contraindicated with administration of MAOI 445 requiring an intervening period of at least 14 days. . . experimentation while the invention provides a predictive strategy for choosing an effective agent. Similarly, WELLBUTRIN, an agent in the sub-class **bupropion** 450 is also contraindicated with MAOI 445 agents. Thus, the ability to prospectively distinguish between such agents enables effective care. . .

DETD . . . atypical cardiac arrhythmias including variants of sinus tachycardia, intermittent sinus tachycardia, sinus bradycardia and sinus arrhythmia, cognitive problems, atypical dermatitis, **depression**, **dissociative** disorders, eating disorders such as bulimia, anorexia and atypical eating disorders, appetite disturbances and weight problems, edema, fatigue, atypical headache. . .

DETD . . . information for a number of therapeutic entities known by their generic names. Examples of such therapeutic entities include: alprazolam, amantadine, **amitriptyline**, atenolol, bethanechol, **bupropion** regular and sustained release tablets, buspirone, carbamazepine, chlorpromazine, chlordiazepoxide, **citalopram**, clomipramine, clonidine, clonazepam, clozapine, cyproheptadine, , deprenyl, desipramine, dextroamphetamine regular tablets and spansules, diazepam, disulfiram, d/l amphetamine, divalproex, doxepin, ethchlorvynol, **fluoxetine**, **fluvoxamine**, felbamate, fluphenazine, gabapentin, haloperidol, **imipramine**, isocarboxazid, lamotrigine, levothyroxine, liothyronine, lithium

carbonate, lithium citrate, lorazepam, loxapine, maprotiline, meprobamate, mesoridazine, methamphetamine, methylphenidate regular and sustained release tablets, midazolam, meprobamate, metoprolol regular and sustained release form, mirtazepine, molindone, moclobemide, **naltrexone**, **nefazodone**, nicotine, **nortriptyline**, olanzapine, oxazepam, **paroxetine**, pemoline, perphenazine, phenelzine, pimozide, pindolol, prazepam, propranolol regular and sustained release tablets, protriptyline, quetiapine, **reboxetine**, risperidone, selegiline, **sertraline**, sertindole, trifluoperazine, trimipramine, temazepam, thioridazine, topiramate, tranylcypromine, trazodone, triazolam, trihexyphenidyl, trimipramine, valproic acid or **venlafaxine**.

DETD . . . the study. TABLE 8 summarizes the composition of the patient population.

TABLE 8

DSM DIRECTED	Number of Patients	Mean/24 h in mg
Fluoxetine	2	40
Nefazodone	1	300
Sertraline	2	175
Clonazepam	1	2
Lithium	2	1050
Valproate	2	1125
Average Number of Medications/Patient	1.8	

DETD [0226]

TABLE 9

DSM + EEG DIRECTED	Number of Patients	Mean/24 h in mg
Valproate	2	1000
Lithium	2	750
Paroxetine	1	30
Fluoxetine	2	35
Methylphenidate	2	27.5
Carbamazepine	2	850
Sertraline	1	100
Average Number of Medications/Patient	1.7	

DETD . . . factors affecting medical condition, atypical asthma and the second treatment is selected from the group consisting of glutamine, phenylalanine, tyrosine, **bupropion**, pamate, moclobemide, phenalazine, seligeline, **venlafaxine**, carbamazapine, gabapentin, lamotrigine, ginko biloba, dextedrine, methamphetamine, methylphenidate, and pemoline.

DETD . . . one of anxiety disorders and the second treatment is selected from the group consisting of gaba, glutamine, phenylalanine, tyrosine, bupropion, **citalopram**, **fluvoxamine**, citalopramine, clomipramine, moclobemide, pamate, phenalazine, seligeline, carbamazapine, divalproex, gabapentin, lamotrigine, guanfacine hcl, clonidine, atenolol, metopolol, propranolol, lithium, ginko biloba, kava. . .

DETD . . . childhood, or adolescence and the second treatment is selected from the group consisting of gaba glutamine, phenylalanine, tyrosine, donepezil, bupropion, **citalopram**, clomipramine, doxepin, **fluoxetine**, **fluvoxamine**, moclobemide, pamate, phenalazine, seligeline, trazodone, **venlafaxine**, carbamazapine, diphenylhydantoin, divalproex, gabapentin, lamotrigine, guanfacine hcl, clorazepate, diazepam, oxazepam, quazepam, atenolol, metopolol, propranolol, lithium, ginko biloba, kava kava, st. . .

DETD . . . the second treatment is selected from the group consisting of

gaba, glutamine, phenylalanine, tyrosine, donepezil, bupropion, moclobemide, pamate, phenalazine, seligeline, **venlafaxine**, carbamazapine, diphenylhydantoin, divalproex, gabapentin, lamotrigine, diazapam, lorazepam, atenolol, metoprolol, propranolol, lithium, ginko biloba, kava kava, st. john's wort, amantadine, phototherapy. . . .

DETD amnestic and other cognitive disorders and the second treatment is selected from the group consisting of glutamine, phenylalanine, tyrosine, donepezil, **amitriptyline**, bupropion, fluxotine, moclobemide, parnate, phenalazine, seligeline, **venlafaxine**, carbamazapine, divalproex, gabapentin, lamotrigine, atenolol, metoprolol, propranolol, lithium, ginko biloba, silbtrimin, amantadine, phototherapy at 10000 lux, zolipidem, adderall, dexedrine, methamphetamine,

DETD disorders not elsewhere classified and the second treatment is selected from the group consisting of glutamine, phenylalanine, tyrosine, donepezil, bupropion, **citalopram**, clomiprimine, desipramine, moclobemide, **nefazodone**, parnate, phenalazine, seligeline, **venlafaxine**, carbamazapine, diphenylhydantoin, divalproex, gabapentin, lamotrigine, guanfacine hcl, clonidine, atenolol, metoprolol, propranolol, ginko biloba, kava kava, silbtrimin, amantadine, phototherapy at 10000. . . .

DETD codes and conditions and the second treatment is selected from the group consisting of gaba, glutamine, phenylalanine, tyrosine, donepezil, bupropion, **citalopram**, clomiprimine, **fluvoxamine**, moclobemide, nortriptyline, parnate, phenalazine, seligeline, trazodone, **venlafaxine**, carbamazapine, divalproex, gabapentin, lamotrigine, guanfacine hcl, clonidine, atenolol, metoprolol, propranolol, ginko biloba, kava kava, st. john's wort, amantadine, phototherapy at. . . .

DETD the second treatment is selected from the group consisting of gaba, glutamine, phenylalanine, tyrosine, donepezil, bupropion, moclobemide, parnate, phenalazine, seligeline, **venlafaxine**, carbamazapine, diphenylhydantoin, divalproex, gabapentin, lamotrigine, diazapam, atenolol, metoprolol, propranolol, lithium, ginko biloba, kava kava, st. john's wort, phototherapy at 10000. . . .

DETD sleep disorders and the second treatment is selected from the group consisting of gaba, glutamine, phenylalanine, tyrosine, donepezil, bupropion, buspirone, **citalopram**, clomiprimine, desipramine, **fluoxetine**, **fluvoxamine**, moclobemide, pamate, phenalazine, seligeline, **sertraline**, **venlafaxine**, carbamazapine, diphenylhydantoin, divalproex, gabapentin, lamotrigine, guanfacine hcl, clonidine, atenolol, metoprolol, propranolol, lithium, ginko biloba, kava kava, st. john's wort, silbtrimin, phototherapy. . . .

DETD of somatoform disorders and the second treatment is selected from the group consisting of gaba, glutamine, phenylalanine, tyrosine, donepezil, bupropion, **citalopram**, **fluvoxamine**, moclobemide, parnate, phenalazine, seligeline, carbamazapine, diphenylhydantoin, divalproex, gabapentin, lamotrigine, atenolol, metoprolol, propranolol, ginko biloba, kava kava, st. john's wort, amantadine,

DETD one of substance-related disorders and the second treatment is selected from the group consisting of gaba, glutamine, phenylalanine, tyrosine, donepezil, **fluvoxamine**, moclobemide, parnate, phenalazine, seligeline, , **venlafaxine**, carbamazapine, diphenylhydantoin, divalproex, gabapentin, lamotrigine, guanfacine hcl, atenolol, metoprolol, propranolol, ginko biloba, kava kava, st. john's wort, silbtrimin, phototherapy at. . . .

DETD Optionally, the treatment modality is drug therapy, and wherein the drug is selected from the group consisting of alprazolam, amantadine, **amitriptyline**, atenolol, bethanechol, **bupropion**, buspirone, carbamazepine, chlorpromazine, chlordiazepoxide, **citalopram**, clomipramine, clonidine, clonazepam, clozapine, cyproheptadine, dexamethasone, divalproex, deprenyl, desipramine, dexamethasone, dextroamphetamine, diazepam, disulfiram, divalproex, doxepin, ethchlorvynol, **fluoxetine**, **fluvoxamine**, felbamate, fluphenazine, gabapentin, haloperidol, **imipramine**, isocarboxazid, lamotrigine, levothyroxine, liothyronine, lithium carbonate, lithium citrate, lorazepam, loxapine, maprotiline, meprobamate, mesoridazine, methamphetamine, midazolam,

meprobamate, **mirtazapine**, molindone, moclobemide, molindone, **naltrexone**, phenelzine, **nefazodone**, **nortriptyline**, olanzapine, oxazepam, **paroxetine**, pemoline, perphenazine, phenelzine, pimozide, pindolol, prazepam, propranolol, protriptyline, quetiapine, **reboxetine**, risperidone, selegiline, **sertraline**, sertindole, trifluoperazine, trimipramine, temazepam, thioridazine, topiramate, tranlycypromine, trazodone, triazolam, trihexyphenidyl, trimipramine, valproic acid, **venlafaxine**, and any combination thereof.

DETD . . . anxiety, panic, and phobic disorders, bipolar disorder, borderline personality disorder, behavior control problems, body dysmorphic disorders, cognitive problems, Creutzfeldt-Jakob disease, **depression**, **dissociative** disorders, eating, appetite, and weight problems, edema, fatigue, hiccups, impulse-control problems, irritability, jet lag, mood problems, movement problems, obsessive-compulsive disorder, . . .

DETD . . . anxiety, panic, and phobic disorders, bipolar disorder, borderline personality disorder, behavior control problems, body dysmorphic disorders, cognitive problems, Creutzfeldt-Jakob disease, **depression**, **dissociative** disorders, eating, appetite, and weight problems, edema, fatigue, hiccups, impulse-control problems, irritability, jet lag, mood problems, movement problems, obsessive-compulsive disorder, . . .

DETD . . . on the CNS system of the patient. And, optionally, the drug is selected from the group consisting of alprazolam, amantadine, **amitriptyline**, atenolol, bethanechol, **bupropion**, buspirone, carbamazepine, chlorpromazine, chlordiazepoxide, **citalopram**, clomipramine, clonidine, clonazepam, clozapine, cyproheptadine, dexamethasone, divalproex, deprenyl, desipramine, dexamethasone, dextroamphetamine, diazepam, disulfiram, divalproex, doxepin, ethchlorvynol, **fluoxetine**, **fluvoxamine**, felbamate, fluphenazine, gabapentin, haloperidol, **imipramine**, isocarboxazid, lamotrigine, levothyroxine, liothyronine, lithium carbonate, lithium citrate, lorazepam, loxapine, maprotiline, meprobamate, mesoridazine, methamphetamine, midazolam, meprobamate, **mirtazapine**, molindone, moclobemide, molindone, **naltrexone**, phenelzine, **nefazodone**, **nortriptyline**, olanzapine, oxazepam, **paroxetine**, pemoline, perphenazine, phenelzine, pimozide, pindolol, prazepam, propranolol, protriptyline, quetiapine, **reboxetine**, risperidone, selegiline, **sertraline**, sertindole, trifluoperazine, trimipramine, temazepam, thioridazine, topiramate, tranlycypromine, trazodone, triazolam, trihexyphenidyl, trimipramine, valproic acid, **venlafaxine**, and any combination thereof.

CLM What is claimed is:

. . . factors affecting medical condition, atypical asthma and the second treatment is selected from the group consisting of glutamine, phenylalanine, tyrosine, **bupropion**, pamate, moclobemide, phenalazine, seligeline, **venlafaxine**, carbamazapine, gabapentin, lamotrigine, ginko biloba, dextedrine, methamphetamine, methylphenidate, and pemoline.

. . . one of anxiety disorders and the second treatment is selected from the group consisting of gaba, glutamine, phenylalanine, tyrosine, bupropion, **citalopram**, **fluvoxamine**, citalopramine, clomipramine, moclobemide, parnate, phenalazine, seligeline, carbamazapine, divalproex, gabapentin, lamotrigine, guanfacine hcl, clonidine, atenolol, metoprolol, propranolol, lithium, ginko biloba, kava. . .

. . . childhood, or adolescence and the second treatment is selected from the group consisting of gaba, glutamine, phenylalanine, tyrosine, donepezil, bupropion, **citalopram**, clomipramine, doxepin, **fluoxetine**, **fluvoxamine**, moclobemide, parnate, phenalazine, seligeline, trazodone, **venlafaxine**, carbamazapine, diphenylhydantoin, divalproex, gabapentin, lamotrigine, guanfacine hcl, clorazepate, diazepam, oxazepam, quazepam, atenolol, metoprolol, propranolol, lithium, ginko biloba, kava kava, st. . .

. . . the second treatment is selected from the group consisting of gaba, glutamine, phenylalanine, tyrosine, donepezil, bupropion, moclobemide,

pamate, phenalazine, seligeline, **venlafaxine**, carbamazapine, diphenylhydantoin, divalproex, gabapentin, lamotrigine, diazapam, lorazepam, atenolol, metoprolol, propranolol, lithium, ginko biloba, kava kava, st. john's wort, amantadine, phototherapy. . . .
 . . . amnestic and other cognitive disorders and the second treatment is selected from the group consisting of glutamine, phenylalanine, tyrosine, donepezil, **amitriptyline**, bupropion, fluxotine, moclobemide, parnate, phenalazine, seligeline, **venlafaxine**, carbamazapine, divalproex, gabapentin, lamotrigine, atenolol, metoprolol, propranolol, lithium, ginko biloba, silbtrimin, amantadine, phototherapy at 10000 lux, zolipidem, adderall, dexedrine, methamphetamine,
 . . . not elsewhere classified and the second treatment is selected from the group consisting of glutamine, phenylalanine, tyrosine, donepezil, bupropion, **citalopram**, clomiprimine, desipramine, moclobemide, **nefazodone**, parnate, phenalazine, seligeline, **venlafaxine**, carbamazapine, diphenylhydantoin, divalproex, gabapentin, lamotrigine, guanfacine hcl, clonidine, atenolol, metoprolol, propranolol, ginko biloba, kava kava, silbtrimin, amantadine, phototherapy at 10000. . . .
 . . . codes and conditions and the second treatment is selected from the group consisting of gaba, glutamine, phenylalanine, tyrosine, donepezil, bupropion, **citalopram**, clomiprimine, **fluvoxamine**, moclobemide, nortriptyline, parnate, phenalazine, seligeline, trazodone, **venlafaxine**, carbamazapine, divalproex, gabapentin, lamotrigine, guanfacine hel, clonidine, atenolol, metoprolol, propranolol, ginko biloba, kava kava, st. john's wort, amantadine, phototherapy at. . . .
 . . . the second treatment is selected from the group consisting of gaba, glutamine, phenylalanine, tyrosine, donepezil, bupropion, moclobemide, pamate, phenalazine, seligeline, **venlafaxine**, carbamazapine, diphenylhydantoin, divalproex, gabapentin, lamotrigine, diazapam, atenolol, metoprolol, propranolol, lithium, ginko biloba, kava kava, st. john's wort, phototherapy at 10000. . . .
 . . . sleep disorders and the second treatment is selected from the group consisting of gaba, glutamine, phenylalanine, tyrosine, donepezil, bupropion, buspirone, **citalopram**, clomiprimine, desipramine, **fluoxetine**, **fluvoxamine**, moclobemide, parnate, phenalazine, seligeline, **sertraline**, **venlafaxine**, carbamazapine, diphenylhydantoin, divalproex, gabapentin, lamotrigine, guanfacine hcl, clonidine, atenolol, metoprolol, propranolol, lithium, ginko biloba, kava kava, st. john's wort, silbtrimin,
 . . . of somatoform disorders and the second treatment is selected from the group consisting of gaba, glutamine, phenylalanine, tyrosine, donepezil, bupropion, **citalopram**, **fluvoxamine**, moclobemide, parnate, phenalazine, seligeline, carbamazapine, diphenylhydantoin, divalproex, gabapentin, lamotrigine, atenolol, metoprolol, propranolol, ginko biloba, kava kava, st. john's wort, amantadine,
 . . . one of substance-related disorders and the second treatment is selected from the group consisting of gaba, glutamine, phenylalanine, tyrosine, donepezil, **fluvoxamine**, moclobemide, parnate, phenalazine, seligeline, , **venlafaxine**, carbamazapine, diphenylhydantoin, divalproex, gabapentin, lamotrigine, guanfacine hcl, atenolol, metoprolol, propranolol, ginko biloba, kava kava, st. john's wort, silbtrimin, phototherapy at. . . .

L14 ANSWER 3 OF 12 ADISCTI COPYRIGHT (C) 2003 Adis Data Information BV on STN
 ACCESSION NUMBER: 2002:5287 ADISCTI
 DOCUMENT NUMBER: 800913675
 TITLE: Short-term treatment of post-traumatic stress disorder with **naltrexone**: an open-label preliminary study.
 ADIS TITLE: **Naltrexone**: therapeutic use.
 Post-traumatic stress disorder.
 AUTHOR: Lubin G; Weizman A; Shmushkevitz M; Valevski A.
 CORPORATE SOURCE: Geha Psychiatric Hospital, Rabin Medical Center, Petah Tikva, Israel.
 SOURCE: Human Psychopharmacology: Clinical and Experimental (Jun 1, 2002), Vol. 17, pp. 181-185
 DOCUMENT TYPE: Study
 REFERENCE: Anxiety Disorders
 FILE SEGMENT: Summary

LANGUAGE: English

WORD COUNT: 558

TI Short-term treatment of post-traumatic stress disorder with
naltrexone: an open-label preliminary study.
ADIS TITLE: **Naltrexone**: therapeutic use.
Post-traumatic stress disorder.

TX Study Message:

Efficacy: **Naltrexone** is not effective in the treatment of
patients with post- traumatic stress disorder.

Tolerability: **Naltrexone** is moderately tolerated in patients
with post- traumatic stress disorder.

TX Results Highlights:

Efficacy: **Naltrexone** was not effective in the treatment of
patients with post-traumatic stress disorder. No clinically significant
effects were observed after 2 weeks of **naltrexone** therapy.

Tolerability: **Naltrexone** was moderately tolerated in patients
with post- traumatic stress disorder. Three of 8 patients could not
tolerate more than 100. . .

TX. . . often resistant to treatment.

It is known that the endogenous opioid system is involved in the
pathogenesis of post-traumatic stress disorder. **Naltrexone** is an
opioid receptor antagonist that is used in the treatment of drug/alcohol
dependence.

This study assessed the efficacy and tolerability of **naltrexone**
in the treatment of patients with post-traumatic stress disorder.

TX Author Comments:

`At present it seems that there is no support for the use of
naltrexone in the treatment of PTSD [post-traumatic stress
disorder] patients.'

TX. . . of > 19. Time since trauma was 2-23 (mean 11) years. Five patients
also had major depressive disorder.

Concomitant medication: diazepam, **fluoxetine**, oxazepam

TX **Naltrexone**

Drug/Treatment	Dose	Route	Frequency	Duration
Naltrexone	50-200 mg/day	PO	not stated	2
weeks				

TX **Naltrexone** was started at 50 mg/day and increased by 50 mg/day
every 2 days to a maximum of 200 mg/day depending on tolerability. Three
patients could only receive **naltrexone** 100 mg/day while 4
patients received 200 mg/day.

TX Results:

Naltrexone (n = 7)				
	baseline	week 1	week 2	week 3
Median scores				
Revised PTSD inventory:				
total	88.4	84.6	33.7	33.0
33.0	33.7			
hyperarousal	32.4	30.7 sup(a)	31.0 sup(b)	31.7
Mean scores				
IES scale:				
total	46.0		43.0 sup(a)	45.6
dissociation	59.3		57.1 sup(b)	
58.6				
HDRS score	25.3		23.9	25.1
HARS score	29.3		27.9 sup(b)	29.6

PTSD = Post-traumatic stress disorder; HDRS = Hamilton **Depression**
Rating Scale; HARS = Hamilton Anxiety Rating Scale.

a p < 0.05 vs baseline; b 0.05 < p < 0.10 vs. . .

SIDE Side Effects Table:

Side effects (patients)	Naltrexone (n = 8)
-------------------------	---------------------------

Weakness/drowsiness 5
Abdominal discomfort/nausea 3
Headache/tremor 1

CT Drug Descriptors: **Naltrexone**, therapeutic use; Drug withdrawal
therapies, therapeutic use; Opioid receptor antagonists, therapeutic use
CT Disease Descriptors: Post traumatic stress disorder, treatment; . . .

L14 ANSWER 4 OF 12 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN

ACCESSION NUMBER: 2002364548 EMBASE

TITLE: [Pain perception in self-injurious syndrome].
PERCEPCION DEL DOLOR EN EL SINDROME DE COMPORTAMIENTO
AUTOLESIONIVO.

AUTHOR: Mendoza Y.; Pellicer F.

CORPORATE SOURCE: Dr. F. Pellicer, Subdireccion de Neurociencias, Inst. Nac.
Psiqu. Ramon de la Fuente, Calzada Mexico-Xochimilco 101,
San Lorenzo Huipulco 14370, Mexico. pellicer@imp.edu.mx

SOURCE: Salud Mental, (2002) 25/4 (10-16).
Refs: 62

ISSN: 0185-3325 CODEN: SAMEF5

COUNTRY: Mexico

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 008 Neurology and Neurosurgery
032 Psychiatry
037 Drug Literature Index

LANGUAGE: Spanish

SUMMARY LANGUAGE: English; Spanish

AB . . . D1 antagonists and 5HT precursors reduced the incidence of SIB,
and NMDA antagonist completely removed it; neither D2 antagonists nor
naloxone affected SIB. It is possible to generate SIB in rats
after inducing peripheral nerve lesions and inflammation process in a . .
. significantly correlated with impulsivity, chronic anger and somatic
anxiety. A significant negative correlation was found with the number of
platelet **imipramine** receptor sites. BPD patients with SIB showed
a blunted prolactin response to meta-chlorophenylpiperazine that appears to
be in inverse relation. . . show lower experimental pain ratings than
BPD patients who do experience pain during SIB. They also exhibit higher
ratings of **depression**, anxiety, impulsiveness, and
dissociation, as well as suicide attempts and childhood sexual
abuse. The abnormal perception of pain in this group of patients may be
related to a tendency to show **dissociative** symptoms. Thus, EEG
theta activity in patients that do not feel pain during SIB, is
significantly correlated with the **Dissociative** Experience Scale
score. Pain perception and **dissociation** Theta rhythm is recorded
in hypnotic states as well as during anticipation and control of painful
stimulation in healthy individuals.. . "indifference to pain". On the
other hand, left prefrontal mechanisms would inhibit the amygdala
resulting in a dampened autonomic output. **Dissociative** symptoms
and SIB in BPD patients are common clinical signs. Besides, BPD patients
show hypometabolism in prefrontal cortical areas and ACC. It is proposed
that the same structures that lead to **dissociative** states may
change the perception of pain by cognitive processes. Conclusions The
authors hypothesize that the structures involved in processing. . .

CT Medical Descriptors:

*pain
*automutilation
dying
psychosis
mental . . .
compound
caffeine
pemoline
amphetamine
n methyl dextro aspartic acid
opiate
serotonin
dopamine 1 receptor blocking agent
serotonin derivative

n methyl dextro aspartic acid receptor blocking agent
dopamine 2 receptor blocking agent

naloxone

endorphin: EC, endogenous compound
opiate derivative: EC, endogenous compound
opiate antagonist
prolactin: EC, endogenous compound

(3 chlorophenyl)piperazine

RN. . . 1200-47-1, 139-10-6, 156-34-3, 2706-50-5, 300-62-9, 51-62-7,
60-13-9, 60-15-1; (n methyl dextro aspartic acid) 6384-92-5; (opiate)
53663-61-9, 8002-76-4, 8008-60-4; (serotonin) 50-67-9; (**naloxone**
) 357-08-4, 465-65-6; (endorphin) 60118-07-2; (prolactin) 12585-34-1,
50647-00-2, 9002-62-4; ((3 chlorophenyl)piperazine) 6640-24-0

L14 ANSWER 5 OF 12 DRUGU COPYRIGHT 2003 THOMSON DERWENT on STN

ACCESSION NUMBER: 2003-25278 DRUGU T

TITLE: Combined treatment with **naltrexone** and EMDR in
patients with severe, post-traumatic stress problems.

AUTHOR: Schillen T B; Luethcke H

LOCATION: Dusseldorf, Ger.

SOURCE: Nervenarzt (73, Suppl. 1, S175, 2002)

CODEN: NERVAF ISSN: 0028-2804

AVAIL. OF DOC.: No Reprint Address.

LANGUAGE: German

DOCUMENT TYPE: Journal

FIELD AVAIL.: AB; LA; CT

FILE SEGMENT: Literature

TI Combined treatment with **naltrexone** and EMDR in patients with
severe, post-traumatic stress problems.

AB. . . case of a young woman with suicidal tendencies and other symptoms
arising from traumatic sexual abuse is reported. Treatment with
mirtazapine + lorazepam + flunitrazepam led to an improvement,
but dissociative symptoms persisted. Additional treatment with
amisulpride had no effect. Subsequently, long-term treatment with
naltrexone combined with EMDR trauma therapy led to satisfactory
long-term stabilization and the patient improved sufficiently to be
released from hospital.. . .

ABEX An 18-yr-old woman with a history of sexual abuse by 5 men at age 12-15
yr presented in a **depressive** state with increasingly suicidal
tendencies. Suicide had been attempted by intoxication and wrist cutting
at age 14 yr, but there. . . was no evidence of drug abuse. Clinical
evaluation revealed sleep disorders, alp-trauma, lack of concentration
and hypervigilance. Initial treatment with **mirtazapine**,
lorazepam and flunitrazepam led to stabilization with improved sleep.
Additional treatment with amisulpride (400 mg/day for 6 wk) had no effect
and subsequently the patient developed increasingly severe
dissociative symptoms with de-realizations, flashbacks and
pseudohallucinations. Supplementary treatment with **naltrexone**
(50 mg/day for 4 wk) led to complete elimination of **dissociative**
symptoms, but anxiety, avoidance behavior, hypervigilance and alp-trauma
persisted. The patient improved and was released from hospital after
trauma-therapy with EMDR, and remained stable 1 yr later during intensive
training and continued treatment with **naltrexone**. (NK/S67)
Kombinationsbehandlung mit Naltrexon und EMDR bei einer Patientin mit
schwerer posttraumatischer Belastungsstörung.

CT [01] **NALTREXONE** *TR; SEVERE *TR; POSTTRAUMATIC *TR; STRESS *TR;
DEPRESSION *TR; MENTAL-DISORDER *TR; **MIRTAZAPINE** *RC;
LORAZEPAM *RC; FLUNITRAZEPAM *RC; AMISULPRIDE *RC; NALTREXON *RN;
CASE-HISTORY *FT; IN-VIVO *FT; EMDR *FT; CASES *FT; ANALGESICS *FT;
MORPHINE-ANTAGONISTS. . . .

L14 ANSWER 6 OF 12 USPATFULL on STN

ACCESSION NUMBER: 2000:137814 USPATFULL

TITLE: Allelic polygene diagnosis of reward deficiency
syndrome and treatment

INVENTOR(S): Blum, Kenneth, San Antonio, TX, United States

PATENT ASSIGNEE(S): City of Hope National Medical Center, Duarte, CA,
United States (U.S. corporation)
The University of Texas System AMD Board of Regents,

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6132724		20001017
APPLICATION INFO.:	US 1998-69886		19980429 (9)
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Witz, Jean C.		
LEGAL REPRESENTATIVE:	Hodgins, Daniel S.		
NUMBER OF CLAIMS:	9		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	8 Drawing Figure(s); 8 Drawing Page(s)		
LINE COUNT:	20845		
SUMM	. . . Volpicelli et al., 1992). Moreover, ethanol-induced increase of brain dopamine levels in animals is blocked by both opiate receptor antagonists naloxone and naltrexone (Widdowson and Holman, 1992; Benjamin et al., 1993). A recent review by Gianoukalis and de Waele (1994) support the role. . .		
SUMM	Pharmacological actions (bromocryptine, bupropion and N-propylnorapomorphine) are partly determined by the individual's dopamine D2 genotype. A1 carriers of the DRD2 gene are pharmacologically more. . .		
DETD	. . . important animal model for RDS behavior. In this regard, various dose regimens and combinations of the three agents (D-phenylalanine [DPA], naltrexone [NTX], Ty-D-Arg [TA]) are being employed against self-selection of either alcohol, cocaine, nicotine, cannabis or sugar. The combination of the. . .		
DETD	. . . salts		
	DPA + Chromium salts		
	NTX + Chromium salts		
	TA + Chromium salts		
	Chromium salts		

DPA = Dphenylalanine; NTX = **naltrexone**; TA = TyD-Arg

DETD . . . Effectiveness Medication

Patients

Physicians Effectiveness

Tropamine

190 17 4.00 Tropamine

150

17 3.50

Buspiran 11 2 4.00 Clonidine 15 2 3.00

Nortriptyline 100 3 4.00 Desipramine 8,824 306 2.84Phenobarbital 2,250 10 4.00 **Imipramine** 2,940 129 2.64"Benzadiazepines" 155 3 3.33 **Fluoxetine** 2,386 145 2.61

Clonidine 412 15 3.33 L-Tyrosine 350 9 2.60

Chlordiazepoxide 510 14 3.25 Carbamazapine 1,384 86 2.57

Diazepam. . . L-Tryptophan 6,247 110 2.20

Amantadine 19,189 225 2.69 Neuroleptics 1,494 54 2.19

Desipramine 10,352 287 2.65 Naltrexone 1,255 40 2.15

Imipramine 2,885 122 2.48 Phenobarbital 100 3 NR

L-Tryptophan 15,112 198 2.33 Composite of 853 47 2.64

Fluoxetine 1,527 111 2.25 "other drugs"

Bupranarphine 148 19 2.00

Naltrexone 817 31 1.68

Mazindol 11 2 1.00

Composite of "other 8,007 119 3.11

drugs'

TOTALS 79,760 468 2.43 TOTALS 37,156. . .

DETD . . . composition is restricted to

the following: Dphenylalanine

500 mg per capsule 6.times. day; TyD-Arg 1 mg per capsule 6.times. day;

Naltrexone 50 mg per capsule 1 to 3 per day.

*GABRB homozygosity of dinucleotide repeat .gtoreq.185 bp

HTR1A TC polymorphism

HTR2A. . .

DETD TABLE 20

Component for Treatment
Composition Contemplated Effective Dose Range

D-phenylalanine

16 to 5000 mg or

Dl-phenylalanine 32 to 10,000 mg

Naltrexone- 1 to 1000 mg

Tyr--Arg 15 .mu.g to 15 mg or Tyr-D-Arg (at same dose range)

Chromium Piccolinate 10 .mu.g. . . .

DETD . . . potentials and to drugs. Facilitation of 5HT release can be accomplished with cocaine, (+)-amphetamine, methamphetamine, fenfluramine, parachloramphetamine, clorimipramine (clomipramine) and **amitriptyline**.

DETD Inhibitors of neuronal uptake of 5HT include the tricyclic anti-depressants (**imipramine**, desimipramine, **amitriptyline**, chlorimipramine, **fluvoxamine**; fenfluramine (an anorectic agent) and cocaine. Any 5HT not bound in storage will be converted into metabolites by MAO. However, . . .

DETD Cocaine also affects opiodergic action. With chronic exposure cocaine to rats, dose-dependent alteration of **naloxone** binding was observed. Opiate receptor density was significantly decreased in several brain structures, while it was increased in the lateral. . . appears that opiate binding was specifically affected in "reward centers" and not in other regions (Hammer et al., 1987). Furthermore, **naloxone**, in another study, effectively blocked the threshold lowering action of cocaine in reward centers of the brain (Bain and Korwetsky, . . .

DETD In this example, the effectiveness of interactions of d-Phenylalanine (other enkephalinase inhibitors), Tyr-D-Arg (an enkephalin releaser) and **Naltrexone** (narcotic antagonist) on the release of dopamine into the nucleus accumbens (Acb) of both the Lewis (polydrug preferring) and the Fischer. . . will be given daily doses of three drugs: 500 mg/kg d-phenylalanine (DPA)-1-5 mg/kg of Tyr-D-Arg (TDA) and 1-2 mg/kg of **naltrexone** (NX) (DuPont, Wilmington, Del.) every morning for 18 days. On the 19th day microdialysis sampling will be begun for either.

DETD Introduction. Over the last decade, a new rapid method to detoxify either methadone or heroin addicts utilizing the narcotic **naltrexone** (Trexan.RTM., Dupont, Del.) sparked interest in many treatment centers throughout the United States, Canada, as well as many other countries. . . .

DETD . . . Gambles as a way of escaping from problems or of relieving a depressed

mood (e.g., feelings of helplessness, guilt, anxiety, **depression**

6. Needs to gamble with increasing amounts of money in order to achieve

the desired excitement

7. After losing money. . . Acts or feels as if the traumatic event were recurring (includes a

sense

of reliving the experience, illusions, hallucinations, and

dissociative

flashback episodes, including those that occur on awakening and when intoxicated.).

4. Has intense psychological distress at exposure to internal. . .

DETD . . . al., 1991) find that luteal phase platelet 5-HT uptake is decreased in women with PMS or PMDD compared with controls.

Imipramine binding sites have also been shown to be reduced in women specifically evaluated for PMDD compared with controls during either. . . .

DETD . . . conducted to evaluate certain psychoactive drugs for the relief of PMDD and includes antidepressants, including clonipramine (Sunblad et al., 1993) **fluoxetine** (Stone et al., 1991; Wood et al., 1992; Steiner et al., 1995; Brandenberg et al.,; Pearlstein and Stone, 1994), **bupropion** (Pearlstein et al., 1995), **paroxetine** (Eriksson et al., 1995; Yonkers et al., 1996a), maprotiline (Eriksson et al., 1995), **sertraline** (Yonkers et al., 1996b), nefaxodone

DETD (Girdler et al., 1995), and fenfluramine (Brzezinski et al., 1990).
 DETD Bain, et al., "Naloxone attenuation of the effect of cocaine
 on rewarding brain stimulation," Life Sciences, 40:1119-1125, 1986.
 DETD Biggio et al., "Stimulation of dopamine synthesis in caudate nucleus by
 intrastriatal enkephalins and antagonism by naloxone,"
 Science, 200:552-54, 1978.
 DETD Ehrenpreis, Balagot, Comaty, Myles, "Naloxone reversible
 analgesia in mice produced by D-phenylalanine and hydrocinnamic acid,
 inhibitors of carboxypeptidase A," In: Bonica et al. (Eds.), Advances.

L14 ANSWER 7 OF 12 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
 ACCESSION NUMBER: 2003072386 EMBASE
 TITLE: Dissociative Identity Disorder: Diagnosis and treatment in
 the Netherlands.
 AUTHOR: Sno H.N.; Schalken H.F.A.
 CORPORATE SOURCE: H.N. Sno, Department of Psychiatry, De Heel General
 Hospital, PO Box 210, 1500 Ee Zaandam, Netherlands
 SOURCE: European Psychiatry, (1999) 14/5 (270-277).
 Refs: 35
 ISSN: 0924-9338 CODEN: EUPSED
 COUNTRY: France
 DOCUMENT TYPE: Journal; Article
 FILE SEGMENT: 017 Public Health, Social Medicine and Epidemiology
 032 Psychiatry
 037 Drug Literature Index

LANGUAGE: English
 SUMMARY LANGUAGE: English

AB **Dissociative** Identity Disorder (DID) is a controversial
 diagnosis and empirical data on the efficacy of treatment modalities are
 scanty. The objective. . . 1:9. The majority of patients were seen once
 a week in an outpatient setting. Individual psychotherapy and adjunctive
 anxiolytic or **antidepressant** medications were the most widely
 endorsed treatment modalities. Hypnosis was rarely used. We conclude that
 the diagnosis of DID is. . .

CT Medical Descriptors:
 *multiple . . . journal
 *anxiolytic agent: DT, drug therapy
 *antidepressant agent: DT, drug therapy
 *anticonvulsive agent: DT, drug therapy
 *neuroleptic agent: DT, drug therapy
 *lithium: DT, drug therapy
 fluoxetine: DT, drug therapy
 paroxetine: DT, drug therapy
 serotonin uptake inhibitor: DT, drug therapy
 clomipramine: DT, drug therapy
 amitriptyline: DT, drug therapy
 tricyclic antidepressant agent: DT, drug therapy
 oxazepam: DT, drug therapy
 alprazolam: DT, drug therapy
 clorazepate: DT, drug therapy
 diazepam: DT, drug therapy
 pimozone: DT, drug therapy
 haloperidol: DT, drug therapy
 thioridazine: DT, drug therapy
 zuclopenthixol: DT, drug therapy
 carbamazepine: DT, drug therapy
 naltrexone: DT, drug therapy

RN (lithium) 7439-93-2; (fluoxetine) 54910-89-3, 56296-78-7,
 59333-67-4; (paroxetine) 61869-08-7; (clomipramine) 17321-77-6,
 303-49-1; (amitriptyline) 50-48-6, 549-18-8; (oxazepam)
 604-75-1; (alprazolam) 28981-97-7; (clorazepate) 20432-69-3, 23887-31-2;
 (diazepam) 439-14-5; (pimozone) 2062-78-4; (haloperidol) 52-86-8;
 (thioridazine) 130-61-0, 50-52-2; (zuclopenthixol) 53772-83-1;
 (carbamazepine) 298-46-4, 8047-84-5; (naltrexone) 16590-41-3,
 16676-29-2

L14 ANSWER 8 OF 12 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
 ACCESSION NUMBER: 1998357499 EMBASE

Added from STIC

TITLE: [Dissociative identity disorder in the Netherlands: A survey of diagnosis and treatment by psychiatrists]. DISSOCIATIEVE IDENTITEITSSTOORNIS IN NEDERLAND: DIAGNOSTIEK EN BEHANDELING DOOR PSYCHIATERS.
AUTHOR: Sno H.N.; Schalken H.F.A.
CORPORATE SOURCE: Dr. H.N. Sno, Afdeling Psychiatrie Stichting, Ziekenhuis 'De Heel', Postbus 210, 1500 EE Zaandam, Netherlands
SOURCE: Tijdschrift voor Psychiatrie, (1998) 40/10 (602-614).
Refs: 28
ISSN: 0303-7339 CODEN: TPSYB3

COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 032 Psychiatry
037 Drug Literature Index
LANGUAGE: Dutch
SUMMARY LANGUAGE: English; Dutch

AB **Dissociative** Identity Disorder is a controversial diagnosis. Few data are available on the efficacy of treatment modalities. A questionnaire has been. . . majority of the patients is seen once a week in an outpatient setting. Conclusion: Individual psychotherapy and adjunctive anxiolytic or **antidepressant** medications are the most widely endorsed treatment modalities. Hypnosis is rarely used. The diagnosis **Dissociative** Identity Disorder could not be dismissed as a nonsensical notion on the part of a small and local sect of. . .

CT Medical Descriptors:
*multiple . . .
DT, drug therapy
*antidepressant agent: DT, drug therapy
*tricyclic antidepressant agent: DT, drug therapy
*serotonin uptake inhibitor: DT, drug therapy
*anticonvulsive agent: DT, drug therapy
 fluoxetine: DT, drug therapy
 paroxetine: DT, drug therapy
clomipramine: DT, drug therapy
 amitriptyline: DT, drug therapy
haloperidol: DT, drug therapy
pimozide: DT, drug therapy
thioridazine: DT, drug therapy
zuclopenthixol: DT, drug therapy
carbamazepine: DT, drug therapy
lithium: DT, drug therapy
oxazepam: DT, drug therapy
alprazolam: DT, drug therapy
diazepam: DT, drug therapy
 naltrexone

RN (fluoxetine) 54910-89-3, 56296-78-7, 59333-67-4; (**paroxetine**) 61869-08-7; (clomipramine) 17321-77-6, 303-49-1; (**amitriptyline**) 50-48-6, 549-18-8; (haloperidol) 52-86-8; (pimozide) 2062-78-4; (thioridazine) 130-61-0, 50-52-2; (zuclopenthixol) 53772-83-1; (carbamazepine) 298-46-4, 8047-84-5; (lithium) 7439-93-2; (oxazepam) 604-75-1; (alprazolam) 28981-97-7; (diazepam) 439-14-5; (**naltrexone**) 16590-41-3, 16676-29-2

L14 ANSWER 9 OF 12 DRUGU COPYRIGHT 2003 THOMSON DERWENT on STN

ACCESSION NUMBER: 1993-06573 DRUGU P

TITLE: Characterization of the Binding of (3H)(+)-Pentazocine to Sigma Recognition Sites in Guinea Pig Brain.

AUTHOR: DeHaven Hudkins D L; Fleissner L C; Ford Rice F Y

CORPORATE SOURCE: Sterling-Winthrop

LOCATION: Malvern, Pennsylvania, United States

SOURCE: Eur.J.Pharmacol.Mol.Pharmacol.Sect. (227, No. 4, 371-78, 1992) 3 Fig. 3 Tab. 43 Ref.

CODEN: EJPPET ISSN: 0922-4106

AVAIL. OF DOC.: Sterling Winthrop Pharmaceuticals Research Division, 25 Great Valley Parkway, Malvern, PA 19355-1314, U.S.A.

LANGUAGE: English

DOCUMENT TYPE: Journal

FIELD AVAIL.: AB; LA; CT; MPC

FILE SEGMENT: Literature

AB. . . of cyclazocine, pentazocine, tonazocine and zenazocine (Sterling-Winthrop), rimcazole (Wellcome), HR-375 (cinuperone, Hoechst-Roussel), BMY-14802 (Bristol-Squibb), dextromethorphan, dextrorphan, PPP-3 (preclamol), 1,3-di(2-tolyl)guanidine, haloperidol, **amitriptyline**, chlorpromazine, **imipramine**, perphenazine, thioridazine, trifluoperazine, triflupromazine, (+)-ethylketo-cyclazocine, GBR-12909, meperidine, morphine, phencyclidine, U-50488H, SCH-23390, SKF-10047, atropine, bethanechol, CPP, apomorphine, d-amphetamine, chlordiazepoxide, clozapine and. . .

ABEX Other drugs studied were (-)-ethylketocyclazocine, glutamate, glycine, methocitramine, MK-801 (dizocilpine), **nalbuphine**, **naloxone**, norbinaltorphimine, pirenzepine, R(-)-quinuclidinylbenzilate, SKF-38393, substance-P, sulpiride, U-69593 and yohimbine. The specific binding of 3H-PE to brain membranes of male Hartley. . . maximal at 37 deg, had a KD of 2.9 nM and Bmax of 1998 fmol/mg protein. The half-life for PE dissociation was 121 min. PE binding was inhibited by Li+, Ca2+ and Mg2+ (10-100 mM), but not by GTP, GDP, GppNhp, . . . for (-)-butaclamol, which was 10-fold more potent than (+)-butaclamol, and (+)-3PPP, which was 9-fold more potent than (-)-3PPP. Antipsychotics and **antidepressants** showed moderate affinity, with the exception of perphenazine. Dextromethorphan and dextrorphan were moderately potent. Sigma reference compounds interacted with the. . .

[01]. . . TONAZOCINE *RC; ZENAZOCINE *RC; RIMCAZOLE *RC; CINUPERONE *RC; BMY-14802 *RC; DEXTROMETHORPHAN *RC; DEXTROPHAN *RC; PRECLAMOL *RC; DITOLYLGUANIDINE-1,3 *RC; HALOPERIDOL *RC; **AMITRIPTYLINE** *RC; CHLORPROMAZINE *RC; **IMIPRAMINE** *RC; PERPHENAZINE *RC; THIORIDAZINE *RC; TRIFLUOPERAZINE *RC; TRIFLUPROMAZINE *RC; ETHYLKETAZOCINE *RC; VANOXERINE *RC; PETHIDINE *RC; MORPHINE *RC; PHENCYCLIDINE *RC; U-50488H. . . BETHANECHOL *RC; CPP *RC; APOMORPHINE *RC; AMPHETAMINE *RC; CHLORDIAZEPOXIDE *RC; CLOZAPINE *RC; GLUTAMATE *RC; GLYCINE *RC; METHOCITRAMINE *RC; DIZOCILPINE *RC; **NALBUPHINE** *RC; **NALOXONE** *RC; BUTACLAMOL *RC; NORBINALTORPHIMINE *RC; PIRENZEPINE *RC; RO-2-3308 *RC; SKF-38393 *RC; SUBSTANCE-P *RC; SULPIRIDE *RC; U-69593 *RC; YOHIMBINE *RC; IN-VITRO.

L14 ANSWER 10 OF 12 DRUGU COPYRIGHT 2003 THOMSON DERWENT on STN

ACCESSION NUMBER: 1988-43513 DRUGU P

TITLE: Tricyclic Antidepressants Block N-Methyl-D-Aspartate Receptors: Similarities to the Action of Zinc.

AUTHOR: Reynolds I J; Miller R J

LOCATION: Chicago, Illinois, United States

SOURCE: Br.J.Pharmacol. (95, No. 1, 95-102, 1988) 3 Fig. 3 Tab. 33

Ref.

CODEN: BJPCBM ISSN: 0007-1188

AVAIL. OF DOC.: Department of Pharmacological and Physiological Sciences, The University of Chicago, 947 E. 58th Street, Chicago, IL 60615, U.S.A.

LANGUAGE: English

DOCUMENT TYPE: Journal

FIELD AVAIL.: AB; LA; CT

FILE SEGMENT: Literature

AB. . . of 3H-MK-801 (Merck-USA) to rat brain membranes was inhibited competitively by cyclazocine, dextromethorphan, ketamine and SKF-10047 and non-competitively by chlorpromazine, **imipramine** (IM), chlorIM (both CIBA-Geigy), **nortriptyline**, amitriptyline, desmethyIM, protriptyline and thioridazine. Carbamazepine, D-amphetamine, mianserin, **fluoxetine**, haloperidol, phenytoin, 5-HT, (+) and (-) oxaprotiline, pargyline, zimelidine, nitrazepam, noradrenaline, maprotiline, dopamine, pentylentetrazol, iprindole, trazodone and **naloxone** were inactive. The MK-801 dissociation rate was slowed by chlorIM, IM and desmethyIM. In cultured rat cortical neurons the Ca influx evoked by N-methyl-D-aspartate (NMDA) was reduced by IM, desmethyIM and ketamine. These data show that tricyclic **antidepressants** act on the Zn site of the NMDA receptor.

ABEX. . . IC50 of cyclazocine, ketamine, desmethyIM and IM were 0.091, 0.83, 13.25 and 27.17 uM, respectively. Binding was also inhibited by **amitriptyline**, chlorpromazine, chlorIM desmethyIM, IM,

nortriptyline, protriptyline and thioridazine with IC50 of 57.25, 45.87, 44.87, 7.41, 22.52, 20.98, 24.9 and 92.45 uM, respectively and Hill slopes somewhat greater than unity. At 100 uM carbamazepine, D-amphetamine, dopamine, **fluoxetine**, haloperidol, iprindol, maprotiline, mianserin, **naloxone**, nitrazepam, noradrenaline, oxaprolidine, pargiline, pentylenetetrazole, phenytoin, 5-HT, trazodone and zimelidine were inactive. The dissociation rate of MK-801 (1/min) was 6250.

CT [06] **IMIPRAMINE** *PH; PSYCHOSTIMULANTS *FT; ANTIDEPRESSANTS *FT; PSYCHOTONICS *FT; IMIPRAMIN *RN; PH *FT
 [07] **CLOMIPRAMINE** *PH; PSYCHOSTIMULANTS *FT; ANTIDEPRESSANTS *FT; CLOMIPRAM *RN; PH *FT
 [08] **NORTRIPTYLINE** *PH; PSYCHOSTIMULANTS *FT; ANTIDEPRESSANTS *FT; NORTRIPTY *RN; PH *FT
 [09] **AMITRIPTYLINE** *PH; PSYCHOSTIMULANTS *FT; ANTIDEPRESSANTS *FT; AMITRIPTY *RN; PH *FT
 [10] **DESIPRAMINE** *PH; PSYCHOSTIMULANTS *FT; ANTIDEPRESSANTS *FT; DESIPRAMI *RN; PH *FT. . . DEXAMPHET *RN; PH *FT
 [15] **MIANSERIN** *PH; PSYCHOSTIMULANTS *FT; ANTIDEPRESSANTS *FT; ANTISEROTONINS *FT; ANTIHISTAMINES-H1 *FT; MIANSERIN *RN; PH *FT
 [16] **FLUOXETINE** *PH; PSYCHOSTIMULANTS *FT; ANTIDEPRESSANTS *FT; FLUOXETIN *RN; PH *FT
 [17] **HALOPERIDOL** *PH; DOPAMINE-ANTAGONISTS *FT; PSYCHOSSEDATIVES *FT; NEUROLEPTICS *FT; HALOPERID *RN; . . . IPRINDOLE *RN; PH *FT
 [29] **TRAZODONE** *PH; PSYCHOSTIMULANTS *FT; ANTIDEPRESSANTS *FT; TRANQUILIZERS *FT; PSYCHOSSEDATIVES *FT; TRAZODONE *RN; PH *FT
 [30] **NALOXONE** *PH; MORPHINE-ANTAGONISTS *FT; NARCOTICS *FT; **NALOXONE** *RN; PH *FT
 [08] **NORTRIPTYLINE** *PH; PSYCHOSTIMULANTS *FT; ANTIDEPRESSANTS *FT; NORTRIPTY *RN; PH *FT
 [09] **AMITRIPTYLINE** *PH; PSYCHOSTIMULANTS *FT; ANTIDEPRESSANTS *FT; AMITRIPTY *RN; PH *FT
 [10] **DESIPRAMINE** *PH; PSYCHOSTIMULANTS *FT; ANTIDEPRESSANTS *FT; DESIPRAMI *RN; PH *FT. . . DEXAMPHET *RN; PH *FT
 [15] **MIANSERIN** *PH; PSYCHOSTIMULANTS *FT; ANTIDEPRESSANTS *FT; ANTISEROTONINS *FT; ANTIHISTAMINES-H1 *FT; MIANSERIN *RN; PH *FT
 [16] **FLUOXETINE** *PH; PSYCHOSTIMULANTS *FT; ANTIDEPRESSANTS *FT; FLUOXETIN *RN; PH *FT
 [17] **HALOPERIDOL** *PH; DOPAMINE-ANTAGONISTS *FT; PSYCHOSSEDATIVES *FT; NEUROLEPTICS *FT; HALOPERID *RN; . . . IPRINDOLE *RN; PH *FT
 [29] **TRAZODONE** *PH; PSYCHOSTIMULANTS *FT; ANTIDEPRESSANTS *FT; TRANQUILIZERS *FT; PSYCHOSSEDATIVES *FT; TRAZODONE *RN; PH *FT
 [30] **NALOXONE** *PH; MORPHINE-ANTAGONISTS *FT; NARCOTICS *FT; **NALOXONE** *RN; PH *FT
 [09] **AMITRIPTYLINE** *PH; PSYCHOSTIMULANTS *FT; ANTIDEPRESSANTS *FT; AMITRIPTY *RN; PH *FT
 [10] **DESIPRAMINE** *PH; PSYCHOSTIMULANTS *FT; ANTIDEPRESSANTS *FT; DESIPRAMI *RN; PH *FT. . . DEXAMPHET *RN; PH *FT
 [15] **MIANSERIN** *PH; PSYCHOSTIMULANTS *FT; ANTIDEPRESSANTS *FT; ANTISEROTONINS *FT; ANTIHISTAMINES-H1 *FT; MIANSERIN *RN; PH *FT
 [16] **FLUOXETINE** *PH; PSYCHOSTIMULANTS *FT; ANTIDEPRESSANTS *FT; FLUOXETIN *RN; PH *FT
 [17] **HALOPERIDOL** *PH; DOPAMINE-ANTAGONISTS *FT; PSYCHOSSEDATIVES *FT; NEUROLEPTICS *FT; HALOPERID *RN; . . . IPRINDOLE *RN; PH *FT
 [29] **TRAZODONE** *PH; PSYCHOSTIMULANTS *FT; ANTIDEPRESSANTS *FT; TRANQUILIZERS *FT; PSYCHOSSEDATIVES *FT; TRAZODONE *RN; PH *FT
 [30] **NALOXONE** *PH; MORPHINE-ANTAGONISTS *FT; NARCOTICS *FT; **NALOXONE** *RN; PH *FT
 [16] **FLUOXETINE** *PH; PSYCHOSTIMULANTS *FT; ANTIDEPRESSANTS *FT; FLUOXETIN *RN; PH *FT
 [17] **HALOPERIDOL** *PH; DOPAMINE-ANTAGONISTS *FT; PSYCHOSSEDATIVES *FT; NEUROLEPTICS *FT; HALOPERID *RN; . . . IPRINDOLE *RN; PH *FT
 [29] **TRAZODONE** *PH; PSYCHOSTIMULANTS *FT; ANTIDEPRESSANTS *FT; TRANQUILIZERS *FT; PSYCHOSSEDATIVES *FT; TRAZODONE *RN; PH *FT
 [30] **NALOXONE** *PH; MORPHINE-ANTAGONISTS *FT; NARCOTICS *FT; **NALOXONE** *RN; PH *FT
 [30] **NALOXONE** *PH; MORPHINE-ANTAGONISTS *FT; NARCOTICS *FT; **NALOXONE** *RN; PH *FT

DDRN . . . OXAPROTIL; CHLORPROM; PARGYLINE; IMIPRAMIN; ZIMELDINE;

CLOMIPRAM; NITRAZPAM; NORTRIPTY; NORADRENA; AMITRIPTY; MAPROTILI;
DESIPRAMI; DOPAMINE; PROTRIPTY; PENTETRAZ; THIORIDAZ; IPRINDOLE;
CARBAMAZE; TRAZODONE; DEXAMPHET; **NALOXONE**; MIANSERIN; FLUOXETIN

L14 ANSWER 11 OF 12 DRUGU COPYRIGHT 2003 THOMSON DERWENT on STN

ACCESSION NUMBER: 1985-08841 DRUGU T P

TITLE: The Analgesic Effects of Tricyclic/Antidepressants: Clinical
and Pharmacological Aspects.

AUTHOR: Devoize J L; Rigal F; Eschallier A; d'Ambrosio A

LOCATION: Clermont-Ferrand, France; Naples, Italy

SOURCE: Presse Med. (13, No. 46, 2806-09, 1984) 31 Ref.

CODEN: PMDAD4

AVAIL. OF DOC.: Service de neurologie, CHU de Clermont-Ferrand, F63000
Clermont-Ferrand, France.

LANGUAGE: French

DOCUMENT TYPE: Journal

FIELD AVAIL.: AB; LA; CT

FILE SEGMENT: Literature

AB Clinical trials of the use of tricyclic antidepressants (e.g.
imipramine, **amitriptyline**) in the treatment of chronic
pain, and hypotheses concerning the possible mechanism of analgesic
action of this group of drugs, . . .

ABEX Results of various clinical studies have confirmed the efficacy of
tricyclic **antidepressants** such as **imipramine**,
clomipramine, **amitriptyline**, desipramine, doxepin, maprotiline,
dibenzepin, in the treatment of chronic pain (lumbalgia, cervicalgia,
rheumatic pain, cancer pain, etc.). The best results. . . been
obtained using relatively high doses of the drugs and in the treatment of
organic pain, particularly peripheral neuropathy. Thus,
imipramine or **amitriptyline** induced improvement in all
cases of diabetic neuropathy whereas diazepam was without effect.
Amitriptyline has proved effective in the treatment of
post-zoster pain. Clomipramine is superior to acetylsalicylic acid in the
treatment of peripheral neuropathies. Hypotheses of the possible
mechanism of the analgesic action of tricyclic **antidepressants**
are discussed. Serotonin, catecholamines and endorphins appear to be
involved. Experimental studies with various drugs (**nortriptyline**
, **protriptyline**, **fluoxetine**, zimelidine, indalpine,
clomipramine, **amitriptyline**, atropine, methysergide,
fenclonine, morphine, **naloxone**, etc.) are reviewed. In
contrast with the slow onset of their **antidepressant** effect,
these drugs promptly relieve pain, suggesting a **dissociation** of
the 2 effects. Combination of tricyclic **antidepressants** with
neuroleptics is contraindicated. (Aspects Cliniques et
Pharmacologiques de l'Effet Antalgique des **Antidépresseurs**
Tricycliques.)

CT [02] **IMIPRAMINE** *TR; **AMITRIPTYLINE** *TR; CLOMIPRAMINE
*TR; DESIPRAMINE *TR; DOXEPIN *TR; MAPROTILINE *TR; DIBENZEPIN *TR;
DIAZEPAM *TR; ASPIRIN *TR; **NORTRIPTYLINE** *PH; PROTRIPTYLINE
*PH; **FLUOXETINE** *PH; ZIMELDINE *PH; INDALPINE *PH;
CLOMIPRAMINE *PH; **AMITRIPTYLINE** *PH; ANALGESIC *FT; PH *FT;
TR *FT
[03] ATROPINE *PH; METHYSERGIDE *PH; FENCLONINE *PH; MORPHINE *PH;
NALOXONE *PH; PH *FT
[03] ATROPINE *PH; METHYSERGIDE *PH; FENCLONINE *PH; MORPHINE *PH;
NALOXONE *PH; PH *FT

L14 ANSWER 12 OF 12 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN

ACCESSION NUMBER: 82090639 EMBASE

DOCUMENT NUMBER: 1982090639

TITLE: High-affinity binding of [3H]doxepin to histamine
H1-receptors in rat brain: Possible identification of a
subclass of histamine H1-receptors.

AUTHOR: Taylor J.E.; Richelson E.

CORPORATE SOURCE: Dept. Psychiat., Mayo Found., Rochester, MN 55905, United
States

SOURCE: European Journal of Pharmacology, (1982) 78/3 (279-285).

CODEN: EJPHAZ

COUNTRY: Netherlands

DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
030 Pharmacology
023 Nuclear Medicine
032 Psychiatry

LANGUAGE: English

AB The binding of the radioactively labeled tricyclic **antidepressant**, [3H]doxepin, to rat brain tissue was examined. Scatchard plots of specific [3H]doxepin binding indicated the presence of two distinct binding sites. The equilibrium **dissociation** constant (K(D)) of the high-affinity site was 0.020 nM with a maximal binding capacity (B(max)) of 13.7 fmol/mg protein. The . . . to the high-affinity H1-receptor, however, was approximately 10% of the B(max) obtained using [3H]pyrilamine to label the H1-receptor. Various tricyclic **antidepressants** were very potent inhibitors at the high-affinity [3H]doxepin site. Their potencies, however, did not correlate with their potencies previously reported. . . .

CT Medical Descriptors:

- *brain
- *central nervous system
- *doxepin h 3
- *mepyramine h 3
- rat
- in vitro study
- animal experiment
- *amitriptyline**
- *antihistaminic agent
- *chlorpheniramine
- *desipramine
- *diazepam
- *diphenhydramine
- *doxepin
- *histamine h1 receptor
- *histamine receptor
- *imipramine**
- *metiamide
- *naloxone**
- *protriptyline
- drug receptor
- radioisotope

RN (**amitriptyline**) 50-48-6, 549-18-8; (chlorpheniramine) 132-22-9; (desipramine) 50-47-5, 58-28-6; (diazepam) 439-14-5; (diphenhydramine) 147-24-0, 58-73-1; (doxepin) 1229-29-4, 1668-19-5; (**imipramine**) 113-52-0, 50-49-7; (metiamide) 34839-70-8; (**naloxone**) 357-08-4, 465-65-6; (protriptyline) 1225-55-4, 438-60-8

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(FILE 'HOME' ENTERED AT 12:55:25 ON 11 SEP 2003)

FILE 'ADISCTI, ADISINSIGHT, ADISNEWS, BIOSIS, BIOTECHNO, CANCERLIT, CAPLUS, CEN, DGENE, DRUGB, DRUGLAUNCH, DRUGMONOG2, DRUGNL, DRUGU, EMBAL, EMBASE, ESBIODBASE, IFIPAT, IPA, JICST-EPLUS, KOSMET, LIFESCI, MEDICONF, MEDLINE, NAPRALERT, NLDB, NUTRACEUT, ...' ENTERED AT 12:55:46 ON 11 SEP 2003

L1 1204255 S DEPRESSI? OR ANTIDERESS? (S) DISSOCIATION
L2 1388563 S DEPRESSI? OR ANTIDEPRESS?
L3 670508 S DISSOCIA?
L4 3968 S L2 (S) L3
L5 411408 S OPIATE? OR OPIOID?
L6 2578933 S ANTAGONIS?
L7 233041 S OPIATE? OR OPIOID? (S) ANTAGONIS?
L8 186472 S NALMEFENE OR NALOXONE OR NALTREXONE OR NALBUPHINE OR THEBAIN
L9 114 S L4 AND L7
L10 253977 S AMITRIPTYLINE OR LOFEPRAMINE OR BUPROPION OR CITALOPRAM OR FL
L11 8 S L9 AND L10
L12 4049 S L10 AND L8
L13 13 S L4 AND L12

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PROCESSING COMPLETED FOR L11

L15 7 DUP REM L11 (1 DUPLICATE REMOVED)

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L15 ANSWER 1 OF 7 IFIPAT COPYRIGHT 2003 IFI on STN DUPLICATE 1

AN 10343482 IFIPAT;IFIUDB;IFICDB

TITLE: TREATMENT OF REFRACTORY DEPRESSION WITH AN
OPIATE ANTAGONIST AND AN ANTIDEPRESSANT

INVENTOR(S): Glover; Hillel, New York, NY, US

PATENT ASSIGNEE(S): Unassigned

AGENT: DICKSTEIN SHAPIRO MORIN & OSHINSKY LLP, 2101 L STREET
NW, WASHINGTON, DC, 20037-1526, US

	NUMBER	PK	DATE
PATENT INFORMATION:	US 2003087896	A1	20030508
APPLICATION INFORMATION:	US 2001-925190		20010809
FAMILY INFORMATION:	US 2003087896		20030508
DOCUMENT TYPE:	Utility		
	Patent Application - First Publication		
FILE SEGMENT:	CHEMICAL APPLICATION		
NUMBER OF CLAIMS:	22		
TI	TREATMENT OF REFRACTORY DEPRESSION WITH AN OPIATE ANTAGONIST AND AN ANTIDEPRESSANT		
AB	An antidepressant or a pharmaceutically acceptable salt thereof, and an opiate antagonist or a pharmaceutically acceptable salt thereof, are used to treat refractory depression characterized by dissociation .		
ECLM	1. A method for treating refractory depression characterized by dissociation , comprising administering to a patient in need thereof an effective dissociation reversing amount of an opiate antagonist or a pharmaceutically acceptable salt thereof; and an effective depression reversing amount of an antidepressant or a pharmaceutically acceptable salt thereof.		
ACLM	2. The method of claim 1, wherein the opiate antagonist is an opiate antagonist having a pentacyclic nucleus. 3. The method of claim 2, wherein the opiate antagonist is selected from the group consisting of nalmefene, naloxone, naltrexone, nalbuphine, thebaine, and combinations thereof. 4. The method of claim 1, wherein the opiate antagonist is selected from the group consisting of kappa opiate antagonists, and combinations thereof. 7. The method of claim 1, wherein the opiate antagonist or pharmaceutically acceptable salt thereof is administered in combination with a pharmaceutically acceptable carrier. 11. The method of claim 1, wherein the antidepressant is selected from the group consisting essentially of amitriptyline , lofepramine , bupropion , citalopram , fluoxetine , fluvoxamine , imipramine , paroxetine , sertraline , venlafaxine , nefazodone , nortriptyline , mirtazapine , reboxetine , SAM-E and combinations thereof. 12. The method of claim 1, wherein the effective depression reversing amount comprises an initial dosage of Bupropion SR in the amount of about 100 mgs. to about 300 mgs. one time daily. 13. The method of claim 1, wherein the effective depression reversing amount comprises a dosage of Venlafaxine in the amount of about 75 mgs. per day to about 375 mgs. one time daily. 14. A method for treating refractory depression characterized by dissociation comprising administering to a patient in need		

thereof an effective amount of (a) an **antidepressant**; and (b) an **opiate** antagonist.

15. The method of claim 14, wherein the **opiate** antagonist is an **opiate** antagonist having a pentacyclic nucleus.

16. The method of claim 14, wherein the **opiate** antagonist is selected from the group consisting of nalmefene, naloxone, naltrexone, nalbuphine, thebaine, and combinations thereof.

18. The method of claim 14, wherein the antidepressant is selected from the group consisting essentially of **amitriptyline**,

lofepramine, **bupropion**, **citalopram**, **fluoxetine**, **fluvoxamine**, **imipramine**, **paroxetine**, **sertraline**, **venlafaxine**, **nefazodone**, **nortriptyline**, **mirtazapine**, **reboxetine**, **SAM-E** and combinations thereof.

19. A method of treating refractory **depression** characterized by **dissociation** comprising administering to a patient in need thereof at least one **opiate** antagonist; evaluating said patient for a response to said **opiate** antagonist; reassessing said patient for **depression**; and administering at least one **antidepressant** to said patient.

20. The method according to claim 19 wherein the step of evaluating said patient for a response to said **opiate** antagonist further comprises the step of evaluating the patient with the Glover Numbing Scale.

21. The method of according to claim 19 wherein the step of evaluating said patient for a response to said **opiate** antagonist further comprises the step of evaluating said patient for responses selected from the group consisting essentially of numb, hollow, . . .

L15 ANSWER 2 OF 7 ADISCTI COPYRIGHT (C) 2003 Adis Data Information BV on STN
ACCESSION NUMBER: 2002:5287 ADISCTI
DOCUMENT NUMBER: 800913675
TITLE: Short-term treatment of post-traumatic stress disorder with
naltrexone: an open-label preliminary study.
ADIS TITLE: Naltrexone: therapeutic use.
Post-traumatic stress disorder.
AUTHOR: Lubin G; Weizman A; Shmushkevitz M; Valevski A.
CORPORATE SOURCE: Geha Psychiatric Hospital, Rabin Medical Center, Petah
Tikva, Israel.
SOURCE: Human Psychopharmacology: Clinical and Experimental (Jun 1,
2002), Vol. 17, pp. 181-185
DOCUMENT TYPE: Study
REFERENCE: Anxiety Disorders
FILE SEGMENT: Summary
LANGUAGE: English
WORD COUNT: 558

TX. . . with antidepressants, benzodiazepines and, on occasion,
antipsychotics. However, many patients are often resistant to treatment.
It is known that the endogenous **opioid** system is involved in the
pathogenesis of post-traumatic stress disorder. Naltrexone is an
opioid receptor **antagonist** that is used in the treatment
of drug/alcohol dependence.

This study assessed the efficacy and tolerability of naltrexone in the
treatment. . .

TX. . . of > 19. Time since trauma was 2-23 (mean 11) years. Five patients
also had major depressive disorder.

Concomitant medication: diazepam, **fluoxetine**, oxazepam

TX. . .	33.7	33.0	33.0	33.7		
hyperarousal			32.4	30.7 sup(a)	31.0 sup(b)	31.7
Mean scores						
IES scale:						
total			46.0		43.0 sup(a)	45.6
dissociation			59.3		57.1 sup(b)	
58.6						
HDRS score			25.3		23.9	25.1
HARS score			29.3		27.9 sup(b)	29.6

PTSD = Post-traumatic stress disorder; HDRS = Hamilton Depression Rating Scale; HARS = Hamilton Anxiety Rating Scale.

a $p < 0.05$ vs baseline; b $0.05 < p < 0.10$ vs. . . .

CT Drug Descriptors: Naltrexone, therapeutic use; Drug withdrawal therapies, therapeutic use; **Opioid receptor antagonists**, therapeutic use

CT Disease Descriptors: Post traumatic stress disorder, treatment; Anxiety, treatment; Anxiety disorders, treatment; Brain disorders, treatment; CNS disorders, . . .

L15 ANSWER 3 OF 7 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN

ACCESSION NUMBER: 2002364548 EMBASE

TITLE: [Pain perception in self-injurious syndrome].
PERCEPCION DEL DOLOR EN EL SINDROME DE COMPORTAMIENTO AUTOLESIVO.

AUTHOR: Mendoza Y.; Pellicer F.

CORPORATE SOURCE: Dr. F. Pellicer, Subdireccion de Neurociencias, Inst. Nac. Psiq. Ramon de la Fuente, Calzada Mexico-Xochimilco 101, San Lorenzo Huipulco 14370, Mexico. pellicer@imp.edu.mx

SOURCE: Salud Mental, (2002) 25/4 (10-16).

Refs: 62

ISSN: 0185-3325 CODEN: SAMEF5

COUNTRY: Mexico

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 008 Neurology and Neurosurgery

032 Psychiatry

037 Drug Literature Index

LANGUAGE: Spanish

SUMMARY LANGUAGE: English; Spanish

AB . . . D1-receptor supersensitivity. Adult rats, when administered high doses of caffeine, pemoline or amphetamine, display SIB. The effects of dopamine, NMDA, **opiate**, and serotonin related agents on acute metamphetamine induced SIB in mice, while D1 antagonists and 5HT precursors reduced the incidence. . . since SIB is necessary to maintain a chronic release of endogenous opioids. This hypothesis is supported by the observation that **opiate** antagonists attenuate severe SIB in a subgroup of autistic patients. The dopaminergic system is believed to be responsible for SIB. . . significantly correlated with impulsivity, chronic anger and somatic anxiety. A significant negative correlation was found with the number of platelet **imipramine** receptor sites. BPD patients with SIB showed a blunted prolactin response to meta-chlorophenylpiperazine that appears to be in inverse relation. . . show lower experimental pain ratings than BPD patients who do experience pain during SIB. They also exhibit higher ratings of **depression**, anxiety, impulsiveness, and **dissociation**, as well as suicide attempts and childhood sexual abuse. The abnormal perception of pain in this group of patients may be related to a tendency to show **dissociative** symptoms. Thus, EEG theta activity in patients that do not feel pain during SIB, is significantly correlated with the **Dissociative** Experience Scale score. Pain perception and **dissociation** Theta rhythm is recorded in hypnotic states as well as during anticipation and control of painful stimulation in healthy individuals. . . "indifference to pain". On the other hand, left prefrontal mechanisms would inhibit the amygdala resulting in a dampened autonomic output. **Dissociative** symptoms and SIB in BPD patients are common clinical signs. Besides, BPD patients show hypometabolism in prefrontal cortical areas and ACC. It is proposed that the same structures that lead to **dissociative** states may change the perception of pain by cognitive processes. Conclusions The authors hypothesize that the structures involved in processing. . .

CT Medical Descriptors:

*pain

*automutilation

dying

psychosis

mental . . . isolation

disease severity

animal behavior

dopaminergic system

denervation
 peripheral nerve injury
 neuritis
 ventral tegmentum
 electrostimulation
 affect
 motivation
 cingulate gyrus
 thalamus anterior nucleus
 learning disorder
 analgesia
 reward
 mood
 Lesch Nyhan syndrome
 human
 nonhuman
 article
 dexamphetamine
 noradrenalin: EC, endogenous compound
 caffeine
 pemoline
 amphetamine
 n methyl dextro aspartic acid
 opiate
 serotonin
 dopamine 1 receptor blocking agent
 serotonin derivative
 n methyl dextro aspartic acid receptor blocking agent
 dopamine 2 receptor blocking agent
 naloxone
 endorphin: EC, endogenous compound
 opiate derivative: EC, endogenous compound
 opiate antagonist
 prolactin: EC, endogenous compound
 (3 chlorophenyl)piperazine

RN. : . . (caffeine) 30388-07-9, 58-08-2; (pemoline) 2152-34-3; (amphetamine)
 1200-47-1, 139-10-6, 156-34-3, 2706-50-5, 300-62-9, 51-62-7, 60-13-9,
 60-15-1; (n methyl dextro aspartic acid) 6384-92-5; (**opiate**)
 53663-61-9, 8002-76-4, 8008-60-4; (serotonin) 50-67-9; (naloxone)
 357-08-4, 465-65-6; (endorphin) 60118-07-2; (prolactin) 12585-34-1,
 50647-00-2, 9002-62-4; ((3 chlorophenyl)piperazine) 6640-24-0

L15 ANSWER 4 OF 7 USPATFULL on STN

ACCESSION NUMBER: 2000:137814 USPATFULL
 TITLE: Allelic polygene diagnosis of reward deficiency
 syndrome and treatment
 INVENTOR(S): Blum, Kenneth, San Antonio, TX, United States
 PATENT ASSIGNEE(S): City of Hope National Medical Center, Duarte, CA,
 United States (U.S. corporation)
 The University of Texas System AMD Board of Regents,
 Austin, TX, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6132724		20001017
APPLICATION INFO.:	US 1998-69886		19980429 (9)
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Witz, Jean C.		
LEGAL REPRESENTATIVE:	Hodgins, Daniel S.		
NUMBER OF CLAIMS:	9		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	8 Drawing Figure(s); 8 Drawing Page(s)		
LINE COUNT:	20845		

SUMM . . . establish some of the brain regions and neurotransmitters
 involved in reward. In particular, it appears that the dependence on
 alcohol, **opiates** and cocaine relies on a common set of
 biochemical mechanisms (Cloninger, 1983; Blum, 1978; Blum, 1989). A
 neuronal circuit deep. . .

SUMM . . . amounts of dopamine from nearby neurons in morphine addicted rats (Nestler et al, 1996). Decreases in D2 receptors observed in **opiate**-dependent subjects have been suggested to indicate that the subjects had low D2 receptors prior to when they began abusing drugs, . . .

SUMM There is evidence that the opiodergic and dopaminergic systems are anatomically and functionally interconnected, suggesting a role for the endogenous **opiodergic** system in mediating the effects of ethanol and other drugs on brain dopaminergic pathways associated with reward. Dopamine **antagonists** and lesions of the dopaminergic pathways in the brain affect pre-proenkephalin A activity (Morris et al., 1988; Normand et al., 1988). Behavioral, pharmacological and neurochemical studies implicate the **opiodergic** and dopaminergic systems in the reinforcing effects of ethanol and other drugs of abuse (Blum et al., 1976a, b; Blum. . . Blum et al., 1977; Blum et al., 1973; Koob and Bloom, 1988; Weiss et al., 1993). Animal studies show that **opiate** receptor agonists increase preference for ethanol, whereas **antagonists** of these receptors reduce ethanol consumption (Blum et al., 1975; Le et al., 1993). Further, studies on animals and human alcoholics suggest the effectiveness of the **opiate** receptor **antagonist** in reducing the positive reinforcing effects of alcohol consumption (O'Malley, 1992; Swift et al., 1994; Blum et al., 1975; Volpicelli et al., 1992). Moreover, ethanol-induced increase of brain dopamine levels in animals is blocked by both **opiate** receptor **antagonists** naloxone and naltrexone (Widdowson and Holman, 1992; Benjamin et al., 1993). A recent review by Gianoukalis and de Waele (1994) support the role of endogenous **opioids** and drugs of abuse (i.e. alcohol).

SUMM Pharmacological actions (bromocryptine, **bupropion** and N-propylnorapomorphine) are partly determined by the individual's dopamine D2 genotype. A1 carriers of the DRD2 gene are pharmacologically more. . . direct microinjection of the D2 agonist N-propylnorapomorphine into the rat nucleus accumbens significantly suppresses the animal's symptoms after withdrawal from **opiates**, while dopamine per se suppresses alcohol withdrawal symptoms (Harris and Aston-Jones, 1994; Blum et al., 1976b). In this regard, there. . . nucleus accumbens and elsewhere in the brain, and it may be that overstimulation of the opioid peptide system by exogenous **opiates** leads to decreases in dopamine function (Pothos et al., 1991). When compared to normal non-alcohol preferring rats, alcohol preferring rats. . .

SUMM . . . appetitive compulsive behaviors are a product of genetic predisposition and environmental insult factors. Numerous studies have implicated the interaction of **opiates**, opioid peptides, CCK-8, glycogen, DA, and insulin in glucose utilization and selective intake of carbohydrates (Morley and Levine, 1988; Moore. . .

SUMM . . . Syndrome (RDS) behaviors in a subject. In certain aspects, this composition includes at least one of the following components: an **opiate** destruction-inhibiting amount of at least one substance which inhibits the enzymatic destruction of a neuropeptidyl **opiate**, the substance being either amino acids, peptides, and structural analogues or derivatives thereof; a neurotransmitter synthesis-promoting amount of at least. . . enkephaline, the enkephaline releaser being, but not limited to, a peptide, and preferably a D-amino acid containing peptide; or an **opiate** antagonist amount of at least one compound which blocks the effects of an **opiate** at either the delta, mu, kappa, sigma, or epsilon receptors. The type of enkephalinase inhibitors, the neurotransmitter precursor, **opiate** destruction-inhibiting substance, **opiate** antagonist, and/or the chromium compound, in addition to the compounds specifically listed above, are further described herein this application and. . .

DETD . . . repeat alleles with a number of different types of drug dependance (cocaine, amphetamine, cannabis), with years of hallucinogen, inhalant, heroin, **opiate**, amphetamine, cocaine, and barbiturate use, with IV drug use and drug overdoses, and with legal problems associated with drug abuse. . .

DETD . . . accumbens, significantly reduces aberrant craving behavior, termed "RDS" behavior, for euphoriant substances to include but not

limited to alcohol, cocaine, **opiates**, nicotine, glucose or other sugars, as well as certain acts such as sexual, gambling, aggression and violence. RDS behaviors have. . .

DETD . . . Effectiveness Medication
Patients
Physicians Effectiveness

Tropamine

190 17 4.00 Trapamine

150

17 3.50

Buspiran 11 2 4.00 Clonidine 15 2 3.00

Nortriptyline 100 3 4.00 Despiramine 8,824 306 2.84

Phenobarbital 2,250 10 4.00 **Imipramine** 2,940 129 2.64

"Benzadiazepines" 155 3 3.33 **Fluoxetine** 2,386 145 2.61

Clonidine 412 15 3.33 L-Tyrosine 350 9 2.60

Chlordiazepoxide 510 14 3.25 Carbamazapine 1,384 86 2.57

Diazepam. . . L-Tryptophan 6,247 110 2.20

Amantadine 19,189 225 2.69 Neuroieptics 1,494 54 2.19

Desipramine 10,352 287 2.65 Naltraxone 1,255 40 2.15

Imipramine 2,885 122 2.48 Phenobarbital 100 3 NR

L-Tryptophan 15,112 198 2.33 Composite of 853 47 2.64

Fluoxetine 1,527 111 2.25 "other drugs"

Bupranarphine 148 19 2.00

Naltrexone 817 31 1.68

Mazindol 11 2 1.00

Composite of "other. . .

DETD . . . disorders. Also, see Tables 17-19 for a brief schematic of how certain elements effect reward induced by stimulants (cocaine, etc.), **opiates** and sedative-hypnotics.

DETD . . . homozygos
ity of the A1 allele)

sedative-hypnotic abuse medical advice rates (AMA), D.sub.2 (Taq A1, B1, exon.sup.6-7 haplotypes, (i.e. alcohol, **opiates**,

improved

physical and BESS C1)

barbiturates) scores

DBPC- DATI VNTR (10/10)

Outpatient CNRI (homozygosity VNTR for <5

bp repeat

MOAA. . . benzodinzipine,

Inpatient OT- DAT1 VNTR(9/9)

withdrawal (including reduced

withdrawal tremors, comparison to

D2 TaqI A1, B1, C1 or exon.sup.6-7

alcohol, **opiates**, reduced depression standard detox haplotype

barbiturates) meds

PHENCAL .TM. Obesity (carbohydrate weight loss, reduced bingeing DBPC -

D.sub.2 Taq1 A1,. . . pain or cramps,

reduced OT Outpatient Same

as for Alcotrol .TM. and

headaches, improved overall Cocotrol .TM.

mood POMC/Pre-

enkephalin/Dynorphin/Orphan

Opiate receptors

delta, sigma, orphan, mu, kappa,

epsilon

.sup.1 Formulas are described in Tables 6 to 17

.sup.2 Alternate composition is. . .

DETD . . . Facilitation

Ventral tegmental area Facilitation

Intracranial Self-Administration

Medial Prefrontal Cortex (Cocaine) Facilitation

Nucleus accumbens (amphetamine) Facilitation

Intravenous Self-Administration

Noradrenaline receptor **antagonists** No change

5-HT receptor **antagonists** Facilitation

M-**opioid** receptor **antagonists** No change
 D.sub.1 and D.sub.2 dopamine receptor **antagonists** Inhibition
 Noradrenaline denervation (6-hydroxydopamine) No change
 5-HT denervation (5,7-dihydroxytryptamine) Facilitation
 Dopamine denervation (6-hydroxydopamine)
 Nucleus accumbens Inhibition
 Ventral tegmental area Inhibition

DETD

TABLE 18

Opiate Reward Paradigm	Effect on Reward
Intracranial Electrical Self-Stimulation	
Lateral hypothalamus Facilitation	
Intracranial Self-Administration	
Nucleus accumbens Facilitation	
Lateral hypothalamus Facilitation	
Ventral tegmental area Facilitation	
Intravenous Self-Administration	
Opioid receptor antagonists	
M-receptor antagonists Inhibition	
.DELTA.-receptor antagonists No change	
K-receptor antagonists No change	
Dopamine receptor antagonists Mixed results	
Dopamine denervation (6-hydroxydopamine)	
Nucleus accumbens No change	

DETD	Reward
Paradigm	Effect on Reward

Intracranial Electrical Self-Stimulation
 Lateral hypothalamus Facilitation
 Intracranial Self-Administration
 Ventral tegmental area Facilitation
 Oral Self-Administration
 GABA.sub.A receptor **antagonists** Inhibition
 GABA.sub.A receptor agonists Facilitation
Opioid receptor **antagonists** Inhibition
 Dopamine receptor **antagonists** Inhibition
 6-HT receptor agonists Inhibition
 Noradrenaline synthesis inhibitors Inhibition

DETD . . . substance and behavioral disorders. Abused substances and behavioral disorders include, but are not limited to, alcohol, cocaine, nicotine, glucose, Cannabis, **opiates** and **opiate** derivatives, gambling, sexual compulsion, hyperactivity, chronic violent behavior and stress disorders, and also symptoms related to premenstrual syndrome (PMS).

DETD . . . drug
 More money spent on All drugs $p < 0.01$ Comings, et
 (including Cocaine and other al., 1994.
 Stimulants, except **opiates**)
 Age of Onset A1 carriers = 23.2 yrs. vs A2 $p < 0.026$ Comings, et
 carriers = 26.7 yrs. al., . . .

DETD . . . potentials and to drugs. Facilitation of 5HT release can be accomplished with cocaine, (+)-amphetamine, methamphetamine, fenfluramine, parachloramphetamine, clorimipramine (clomipramine) and **amitriptyline**.

DETD Inhibitors of neuronal uptake of 5HT include the tricyclic anti-depressants (**imipramine**, desimipramine, **amitriptyline**, chlorimipramine, **fluvoxamine**; fenfluramine (an anorectic agent) and cocaine. Any 5HT not bound in storage will be converted into metabolites by MAO. However, . . .

DETD Enhancer/Releaser of Opioid Peptides An aspect of this invention is the use of substances which inhibit the destruction of neuropeptidyl **opiates**. These **opiates** promote the synthesis and release of dopamine. It has been shown that the administration of **opiate**-like substances to animals increases the rate or striatal

DA biosynthesis and metabolism, an effect which is mediated by special **opiate** receptors located on nigrostriatal dopaminergic terminals (Clouet et al., 1970; Biggio et al., 1978; Regiawi, 1980). Upon chronic administration of.

DETD Cocaine also affects opiodergic action. With chronic exposure cocaine to rats, dose-dependent alteration of naloxone binding was observed. **Opiate** receptor density was significantly decreased in several brain structures, while it was increased in the lateral hypothalamus. It appears that **opiate** binding was specifically affected in "reward centers" and not in other regions (Hammer et al., 1987). Furthermore, naloxone, in another. . . in reward centers of the brain (Bain and Korwetsky, 1987). Moreover, cocaine appears to affect the analgesic action of certain **opiates** (Misra et al., 1987). The inventors believe that the reinforcing action of cocaine may be mediated in part by **opiate** systems in brain reward centers, which are altered by chronic cocaine exposure.

DETD Narcotic drugs were found to act at various "**opiate** receptors." The brain and other nervous tissue were found to possess endogenous opioids (EO). The related pentapeptides, methionine and leucine-enkephalin. . .

DETD . . . abstinence, similar to those produced by narcotic analgesic drugs when the EO's are administered to man or animals. The endogenous **opiates**, like the narcotic drugs, are members of the class "opioids." Enzymes which degrade enkephalins (E5) are generally called "enkephalinases."

DETD . . . rationale for this is that by doing so the inventors could significantly enhance the effect of enkephalin on its respective **opiate** receptor sites (e.g., delta or mu). To accomplish this aim the inventors would prefer to use the peptide Tyr-Arg (Kyotorphin), .

DETD The use of these precursors may be supplemented at appropriate stages of treatment with dopaminergic releasers, blockers, agonists or **antagonists**, or agents affecting the reuptake or degradation of dopamine, norepinephrine or epinephrine. However, and more importantly, the entire range of dopaminergic activity including synthesis, and release is regulated to some degree by certain **opioid** peptides (e.g., enkephalins and endorphins). Centrally administered **opioid** peptides (endorphins and enkephalins) produce elevations in levels of catecholamines in blood plasma in animals and humans (Clouet, 1982). In. . .

DETD . . . use of specific substances, questions were asked about the lifetime use (in years) of alcohol use to intoxication, heroin, other **opiates**/analgesics, barbiturates, other sedatives/hypnotic/tranquilizers, cocaine, amphetamines, cannabis, hallucinogens, and inhalants. For each of the above, where relevant, the subjects were asked. . .

DETD . . . 6.3 58 15.5 38 18.4 6.88 .009
Alcohol dep 160 6.3 98 24.5 22 9.1 non-linear
only

*OSH = other **opiates** (than heroin or methadone), sedatives and hypnotics

DETD . . . herein. Also, see Tables 17-19 for a brief schematic of how certain elements effect reward induced by stimulants (cocaine, etc.), **opiates** and sedative-hypnotics. Specific examples of the method of treatment combined with genetic diagnosis for RDS behaviors is described below:

DETD EXAMPLE OF ANTI-CRAVING COMPOSITION AND ENHANCEMENT OF COMPLIANCE TO TREXAN.RTM. FOLLOWING RAPID DETOXIFICATION FROM **OPIATES** IN HARDCORE ADDICTS

DETD . . . throughout the United States, Canada, as well as many other countries on a worldwide basis. The dropout rate among hardcore **opiate** addicts even today approaches 90 percent. The basic concept in this rapid method is to provide the patient with a pure narcotic antagonist to block the **opiate**-induced euphoriant effects. Utilizing this approach most patients do not comply and the recidivism rate is over 99% (S. Hall, San. . . contention that the major reason for non-compliance is due to the fact that while the narcotic antagonist (Trexan.RTM.) blocks the **opiate** or

alcohol-induced euphoria (O'Malley et al., 1992; Volpicelli et al., 1992), the drug has little effect on craving behavior. Since . . .

DETD . . . into the study included both male and female patients who were considered hardcore addicts as diagnosed utilizing DSM III for heroin/**opiate** dependence. Each patient was pre-evaluated by first receiving an injection of 0.4-0.8 mg. Narcan and their withdrawal was assessed (if. . .

DETD Conclusion It is suggested that the addition of the anti-craving formula significantly reduced the craving for **opiates** and, therefore, seems to be important in assisting those hardcore **opiate** addicts in preventing relapse--especially in conjunction with the narcotic antagonist Trexan.RTM..

DETD . . . Gambles as a way of escaping from problems or of relieving a depressed mood (e.g., feelings of helplessness, guilt, anxiety, **depression**

6. Needs to gamble with increasing amounts of money in order to achieve the desired excitement

7. After losing money. . . Acts or feels as if the traumatic event were recurring (includes a sense of reliving the experience, illusions, hallucinations, and **dissociative** flashback episodes, including those that occur on awakening and when intoxicated.).

4. Has intense psychological distress at exposure to internal. . .

DETD . . . use of specific substances, questions were asked about the lifetime use (in years) of alcohol use to intoxication, heroin, other **opiates**/analgesics, barbiturates, other sedatives/hypnotics/tranquilizers, cocaine, amphetamines, cannabis, hallucinogens, and inhalants.

DETD . . . 58 15.5 38 18.4 6.88 0.009

Alcohol dep. 160 6.3 98 24.5 22 9.1 non-linear only

.sup.a OSH = other **opiates** (than heroin or methadone), sedatives and hypnotics.

DETD Invoking a hypothesis that premenstrual symptoms are induced by withdrawal of endogenous **opiates**, several groups have evaluated .beta.endorphin levels in symptomatic women and controls. In a study that included women who retrospectively reported. . .

DETD . . . al., 1991) find that luteal phase platelet 5-HT uptake is decreased in women with PMS or PMDD compared with controls. **Imipramine** binding sites have also been shown to be reduced in women specifically evaluated for PMDD compared with controls during either. . .

DETD . . . conducted to evaluate certain psychoactive drugs for the relief of PMDD and includes antidepressants, including clonipramine (Sunblad et al., 1993) **fluoxetine** (Stone et al., 1991; Wood et al., 1992; Steiner et al., 1995; Brandenberg et al.,; Pearlstein and Stone, 1994), **bupropion** (Pearlstein et al., 1995), **paroxetine** (Eriksson et al., 1995; Yonkers et al., 1996a), maprotiline (Eriksson et al., 1995), **sertraline** (Yonkers et al., 1996b), nefaxodone (Girdler et al., 1995), and fenfluramine (Brzezinski et al., 1990).

DETD Blum, Hamilton, Wallace, Alcohol and **opiates**: A review of common neurochemical and behavioral mechanisms, Editor: K. Blum, (pp. 203), Academic Press, New York, 1977.

DETD Blum, "A commentary on neurotransmitter restoration as a common mode of treatment for alcohol, cocaine and **opiate** abuse," Integrative Psychiatry, 6:199-204, 1989a.

DETD Li and Chung, "Isolation and Structure of an Untriakontapeptide with **Opiate** Activity from Camel Pituitary Glands," Proc. Nat. Acad. Sci. USA; 73:1145-1148, 1976.

DETD Misra, et al.,; "Stereospecific potentiation of **opiate** analgesia by cocaine: Predominant role of noradrenaline," Pain., 28:129-138, 1987.

CLM What is claimed is:

1. A composition comprising a) an **opiate** destruction-inhibiting amount of at least one substance which inhibits the enzymatic

destruction of a neuropeptidyl **opiate**, said substance being selected from the group consisting of amino acids, peptides, and analogues or derivatives of amino acids or. . .

8. The composition of claim 1 where the **opiate** is a peptide.

9. The composition of claim 1 where the **opiate** is an enkephalin.

L15 ANSWER 5 OF 7 USPATFULL on STN

ACCESSION NUMBER: 2000:80744 USPATFULL

TITLE: Methods and compositions for treating and preventing anxiety and anxiety disorders using optically pure (R) tofisopam

INVENTOR(S): Landry, Donald W., New York, NY, United States
Klein, Donald F., New York, NY, United States

PATENT ASSIGNEE(S): Janus Pharmaceuticals, Inc., New York, NY, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6080736		20000627
APPLICATION INFO.:	US 1999-429503		19991027 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 1998-105803P	19981027 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	Granted	
PRIMARY EXAMINER:	Henley, III, Raymond	
LEGAL REPRESENTATIVE:	Fish & Neave, Haley, Jr., James F., Shin, Elinor K.	
NUMBER OF CLAIMS:	37	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	4 Drawing Figure(s); 3 Drawing Page(s)	
LINE COUNT:	1332	

SUMM In some cases, enantiomers can have opposite pharmacological effects. The (+) enantiomer of piconadol is an agonist at the **opioid** receptor while the (-) enantiomer acts as an **antagonist** at the same receptor. Powell et al. In: Wainer I W, Drager D E, editors, Drug Stereochemistry Analytical Methods and. . . have opposite actions on the receptor. The S-enantiomers are potent activators at L-type voltage-dependant calcium channels whereas the R-enantiomers are **antagonists**. Triggle, D. J. Chirality, 1994: 6:58-62.

SUMM The essential feature of this syndrome is the development of **dissociative** symptoms along with symptoms similar to those of PTSD as a result of exposure to a traumatic event. Individuals with. . . Acute Stress Disorder may neglect basic health and safety needs and are at increased risk of developing PTSD and Major **Depression**.

DETD . . . before, along with, or after other psychoactive compounds, particularly those with antidepressant activity. Such compounds include tricyclic antidepressants such as **amitriptyline**, clomipramine, doxepin, **imipramine**, trimipramine, amoxapine, desipramine, maprotiline, **nortriptyline**, and protryptiline; serotonin-reuptake inhibitors such as racemic **fluoxetine** and enantiomers, **fluvoxamine**, **paroxetine**, **sertraline**, and (.+-.)-**venlafaxine**; atypical antidepressants such as **bupropion**, **nefazodone**, and trazodone; and other monoamine oxidase inhibitors, such as phenelzine, tranylcypromine, and (-)-**selegiline**, either singly or in combination. In particular,. . .

CLM What is claimed is:
14. The method of claim 13 wherein the tricyclic antidepressant is selected from the group consisting of **amitriptyline**, clomipramine, doxepin, **imipramine**, (+)-trimipramine, amoxapine, desipramine, maprotiline, **nortriptyline**, and protryptiline.

15. The method of claim 12 wherein the antidepressant is selected from the group consisting of **fluoxetine**, **fluvoxamine**,

paroxetine, sertraline, (.+-.)-venlafaxine,
bupropion, nefazodone, trazodone, phenelzine,
tranylcypromine, (-)-selegiline and moclobemide.

L15 ANSWER 6 OF 7 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
ACCESSION NUMBER: 94196592 EMBASE
DOCUMENT NUMBER: 1994196592
TITLE: Pharmacotherapy for post-traumatic stress disorder.
AUTHOR: Sutherland S.M.; Davidson J.R.T.
CORPORATE SOURCE: Department of Psychiatry, Duke University Medical Center,
Box 3812, Durham, NC 27710, United States
SOURCE: Psychiatric Clinics of North America, (1994) 17/2
(409-423).
ISSN: 0193-953X CODEN: PCAMDG
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 032 Psychiatry
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB . . . or develop a consensus that is well supported by research findings. What has emerged from the available data is that **antidepressants**, particularly those with serotonergic properties, are helpful for core PTSD symptoms when given at higher dose levels for at least. . . weeks. The TCAs as a group appear to be effective in amelioration of the intrusive symptoms and of anxiety and **depressive** symptoms, while having little effect on avoidance symptoms. Initial data from studies of the SSRIs suggests that they may have. . . in PTSD symptoms that some patients will no longer meet the diagnostic criteria. The hyperarousal symptoms may respond somewhat to **antidepressants**, but should symptoms continue to be disabling, buspirone or benzodiazepines may be indicated. In choosing a benzodiazepine, those less likely. . . For some patients, phenelzine may be a good choice because it has proven efficacy for the intrusive PTSD symptoms, for **depressive** symptoms, and for some symptoms of autonomic arousal, such as panic attacks. Other agents to be considered for alleviation of. . . impulse control, lithium, beta-blocking drugs, and carbamazepine may be helpful. Brief psychotic episodes should respond to a neuroleptic, although psychoticlike **dissociative** spells may be nonresponsive.

CT Medical Descriptors:

*posttraumatic . . .
therapy

alprazolam: DT, drug therapy

carbamazepine: DT, drug therapy

clonazepam: DT, drug therapy

clonidine: DT, drug therapy

corticotropin releasing factor: EC, endogenous compound

dopamine: EC, endogenous compound

fluoxetine: DT, drug therapy

fluvoxamine: DT, drug therapy

neuroleptic agent: DT, drug therapy

opiate derivative: EC, endogenous compound

phenelzine: DT, drug therapy

propranolol: DT, drug therapy

serotonin: EC, endogenous compound

sertraline: DT, drug therapy

valproic acid: DT, drug therapy

RN (alprazolam) 28981-97-7; (carbamazepine) 298-46-4, 8047-84-5; (clonazepam) 1622-61-3; (clonidine) 4205-90-7, 4205-91-8, 57066-25-8; (corticotropin releasing factor) 9015-71-8; (dopamine) 51-61-6, 62-31-7; (**fluoxetine**) 54910-89-3, 56296-78-7, 59333-67-4; (**fluvoxamine**) 54739-18-3; (phenelzine) 156-51-4, 51-71-8; (propranolol) 13013-17-7, 318-98-9, 3506-09-0, 4199-09-1, 525-66-6; (serotonin) 50-67-9; (**sertraline**) 79617-96-2; (valproic acid) 1069-66-5, 99-66-1

L15 ANSWER 7 OF 7 ADISNEWS COPYRIGHT (C) 2003 Adis Data Information BV on STN

ACCESSION NUMBER: 1997:10 ED: 8 Aug 2001 UP: 8 Aug 2001
DOCUMENT NUMBER: 11738324-800458311
TITLE: Reviews: Headline news of 1996 - Part 3.
SOURCE: INPHARMA 10 Jan 1997 ISSN: 1173-8324
DOCUMENT TYPE: (MIX)
WORD COUNT: 1137

TX. . . local anaesthetic to be used when profound muscle relaxation is required during surgery. Also, low-dose ropivacaine is associated with greater **dissociation** of the sensory and motor effects of local anaesthesia, compared with other local agents such as bupivacaine; this allows for. . . the agent are currently underway. Remifentanil ['Ultiva'; Glaxo Wellcome], the first of a new class of anaesthetic drugs called the esterase-metabolised **opioids**, was approved in its first market, Germany, last year. Remifentanil is indicated for use during the induction and maintenance of. . . the end of 1996, and was subsequently launched in UK in October. The use of alternative medicines in the treatment of **depression** was another focus of 1996. In particular, interest has centred on extracts of St John's Wort (*Hypericum perforatum*). A meta-analysis of randomised trials involving patients with anxiety, **depressive** and sleep disorders indicated a response rate of 55% to *Hypericum perforatum* therapy, compared with a response rate of 22% with placebo. The response rate achieved with *Hypericum perforatum* therapy was comparable to that achieved with conventional **antidepressants**. Another study, involving 165 patients with **depression** demonstrated that hypericum extract [LI-160; Lichtwer Pharmaceuticals] had comparable **antidepressant** activity to **amitriptyline** after 6 weeks' therapy. Furthermore, hypericum extract was shown to have a better tolerability profile than **imipramine** in another 209-patient study.
GENITOURINARY MEDICINE

Merck & Co. contested the results of a study, published in 1996, which showed that their. . . postmenopausal women with RA. Nine women received intra- articular injections of genetically altered synovial cells that express an IL-1 receptor **antagonist**. T-cell receptor Vbeta17 peptide vaccine [Immune Response; phase I/II] was also under investigation in patients with RA. The 15 vaccine recipients.

RN 50-48-6 (**AMITRIPTYLINE**)
50-49-7 (**IMIPRAMINE**)
52-86-8 (**HALOPERIDOL**)
8001-02-3 (**CORTICOSTEROIDS**)
38396-39-3 (**BUPIVACAINE**)
63590-64-7 (**TERAZOSIN**)
66376-36-1 (**ALENDRONIC ACID**)
71125-38-7 (**MELOXICAM**)
84057-95-4 (**ROPIVACAINE**)
89957-37-9 (**ANTIBODIES**)
98319-26-7 (**FINASTERIDE**)
106516-24-9. . .

=> s psychosis

L16 152084 PSYCHOSIS

=> s refractory depression

L17 1677 REFRACTORY DEPRESSION

=> s l16 and l17

29 FILES SEARCHED...

L18 129 L16 AND L17

=> d his

(FILE 'HOME' ENTERED AT 12:55:25 ON 11 SEP 2003)

FILE 'ADISCTI, ADISINSIGHT, ADISNEWS, BIOSIS, BIOTECHNO, CANCERLIT, CAPLUS, CEN, DGENE, DRUGB, DRUGLAUNCH, DRUGMONOG2, DRUGNL, DRUGU, EMBAL,

EMBASE, EMBASE, IFIPAT, IPA, JICST-EPLUS, KOSMET, LIFESCI, MEDICINF,
MEDLINE, NAPRALERT, NLDB, NUTRACEUT, ...' ENTERED AT 12:55:46 ON 11 SEP
2003

L1 1204255 S DEPRESSI? OR ANTIDERESS? (S) DISSOCIATION
L2 1388563 S DEPRESSI? OR ANTIDEPRESS?
L3 670508 S DISSOCIA?
L4 3968 S L2 (S) L3
L5 411408 S OPIATE? OR OPIOID?
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L17 1677 S REFRACTORY DEPRESSION
L18 129 S L16 AND L17

=> s l16 (s) l17

L19 5 L16 (S) L17

=> s l7 and l19

L20 0 L7 AND L19

=> s l18 and l7

L21 1 L18 AND L7

=> d l21 ibib, kwic

L21 ANSWER 1 OF 1 DRUGU COPYRIGHT 2003 THOMSON DERWENT on STN

ACCESSION NUMBER: 2000-01884 DRUGU T

TITLE: Treatment augmentation with **opiates** in severe and
refractory major depression.

AUTHOR: Stoll A L; Rueter S

LOCATION: Belmont, Mass., USA

SOURCE: Am.J.Psychiatry (156, No. 12, 2017, 1999) 2 Ref.

CODEN: AJPSAO ISSN: 0002-953X

AVAIL. OF DOC.: No Reprint Address.

LANGUAGE: English

DOCUMENT TYPE: Journal

FIELD AVAIL.: AB; LA; CT

FILE SEGMENT: Literature

TI Treatment augmentation with **opiates** in severe and refractory
major depression.

AB 3 Cases of **refractory depression** treated with the mu
opiate agonists oxycodone and oxymorphone were reported in a
letter. Patients with **refractory depression** reported
lifting of symptoms during **opiate** abuse or treatment. Their
depression responded well to supervised oxycodone or oxymorphone
treatment. **Opiates** should be considered in carefully selected
patients with severe, **refractory depression**.

ABEX. . . A 44-yr-old man with severe, chronic depression had not responded
well to antidepressant treatment. He also had a history of **opiate**
abuse and reported a lack of depression whilst using **opiates**.
He was given a trial of oxycodone 10 mg/day under supervision, and
remained in remission from depression after 18 mth, without emergence of
opiate abuse or tolerance. A 45-yr-old woman with a history of
bipolar disorder and **opiate** abuse (in remission for 2 yr)
showed a lack of response to mood stabilizers, and emergence of mania
under standard antidepressant treatment. She reported feeling well when
taking **opiates**, particularly oxymorphone. Oxymorphone 8 mg/day
was added to lamotrigine therapy, and she remained well for 20 mth
without emergence of **opiate** abuse or tolerance. A 43-yr-old man
with a history of chronic major depression refractory to antidepressants,
reported that he had shown marked improvement whilst receiving

opiates after a dental procedure. He was started on oxycodone 10 mg t.i.d. for 9 mth, and showed a marked antidepressant response without opiate abuse or tolerance. (KO)

CT DEPRESSION *TR; REFRACTORY *TR; BIPOLAR *TR; **PSYCHOSIS** *TR;
MENTAL-DISORDER *TR; CASE-HISTORY *FT; IN-VIVO *FT; NARCOTIC *FT;
ANTIDEPRESSANT *FT; ADDICTION *FT; CASES *FT; PSYCHOSTIMULANT *FT
CT DEPRESSION *TR; REFRACTORY *TR; BIPOLAR *TR; **PSYCHOSIS** *TR;
MENTAL-DISORDER *TR; CASE-HISTORY *FT; IN-VIVO *FT; NARCOTIC *FT;
ANTIDEPRESSANT *FT; ADDICTION *FT; CASES *FT; PSYCHOSTIMULANT *FT

=> dup rem

ENTER L# LIST OR (END):119

DUPLICATE IS NOT AVAILABLE IN 'ADISINSIGHT, ADISNEWS, DGENE, DRUGLAUNCH, DRUGMONOG2, KOSMET, MEDICONF, NUTRACEUT, PCTGEN, PHARMAML'.

ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE

PROCESSING COMPLETED FOR L19

L22 5 DUP REM L19 (0 DUPLICATES REMOVED)

=> d l22 1-5 ibib, kwic

L22 ANSWER 1 OF 5 USPATFULL on STN

ACCESSION NUMBER: 2002:228330 USPATFULL

TITLE: Combination treatment for anxiety, depression, obsessive compulsive disorder and psychosis

INVENTOR(S): Howard, Harry R., JR., Bristol, CT, UNITED STATES

PATENT ASSIGNEE(S): Pfizer Inc. (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002123490	A1	20020905
APPLICATION INFO.:	US 2001-10651	A1	20011206 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-272619P	20010301 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	PFIZER INC, 150 EAST 42ND STREET, 5TH FLOOR - STOP 49, NEW YORK, NY, 10017-5612	

NUMBER OF CLAIMS: 30

EXEMPLARY CLAIM: 1

LINE COUNT: 1659

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM [0006] This invention also relates to a method of treating OCD, **psychosis** and depression in a mammal, comprising administering to said mammal: (a) a serotonin reuptake inhibitor (SRI) compound that exhibits activity. . . and "b" above are present in amounts that render the combination of the two agents effective in treating, respectively, OCD, **psychosis** and depression with improvement in the efficacy achieved by either component individually in the treatment of OCD, depression, especially **refractory depression**, and **psychosis**.

SUMM . . . invention that contain an atypical antipsychotic agent and an SRI antidepressant are useful for the treatment of OCD, depression, especially **refractory depression**, or **psychosis**, especially schizophrenia. As used herein, the term "depression" includes depressive disorders, for example, single episodic or recurrent major depressive disorders, . . .

SUMM [0010] The compositions of the present invention are especially useful for the treatment of depression, especially **refractory depression** where the use of an antidepressant is generally prescribed. By the use of a combination of an atypical antipsychotic agent and an SRI antidepressant agent in accordance with the present invention, it is possible to treat depression, especially **refractory depression**, in patients for whom conventional antidepressant therapy might not be wholly successful or where OCD or **psychosis**, especially schizophrenia, are present.

L22 ANSWER 2 OF 5 DRUGU COPYRIGHT 2003 THOMSON DERWENT on STN

ACCESSION NUMBER: 2002-46795 DRUGU T

TITLE: The influence of clinical features of refractory depression on antidepressant treatment results.

AUTHOR: Hese R T; Gruszczynski W; Szwed A; Kielc M; Zalitacz M

CORPORATE SOURCE: Univ.Silesian

LOCATION: Katowice, Lodz; Bytom, Pol.

SOURCE: Pharmacopsychiatry (35, No. 5, III, 2002) 1 Ref.

CODEN: PHRMEZ ISSN: 0176-3679

AVAIL. OF DOC.: Silesian University School of Medicine, Department of Psychiatry, Katowice, Poland.

LANGUAGE: English

DOCUMENT TYPE: Journal

FIELD AVAIL.: AB; LA; CT

FILE SEGMENT: Literature

AB The therapeutic efficacy of amitriptyline (AMI), mianserin (MIA) and ECT were compared in 180 patients with **refractory depression** treated at a Polish hospital. Patients with moderate depression, **psychosis**-free depression and depression with inhibition features had better therapeutic results than those with severe depression, psychotic depression and depression with. . .

L22 ANSWER 3 OF 5 DRUGU COPYRIGHT 2003 THOMSON DERWENT on STN

ACCESSION NUMBER: 2000-22698 DRUGU T

TITLE: Treatment-refractory depression successfully treated with the combination of mirtazapine and lithium.

AUTHOR: Moustgaard G

LOCATION: Helsingborg, Swed.

SOURCE: J.Clin.Psychopharmacol. (20, No. 2, 268, 2000) 7 Ref.

CODEN: JCPYDR ISSN: 0271-0749

AVAIL. OF DOC.: S-25187 Helsingborg, Sweden.

LANGUAGE: English

DOCUMENT TYPE: Journal

FIELD AVAIL.: AB; LA; CT

FILE SEGMENT: Literature

AB A case of **refractory depression** successfully treated with the combination of mirtazapine (MZ) and lithium (Li) in a patient, who was previously treated with several. . . and was treated with the combination of amitriptyline and neuroleptics. After several yr, the patient was again admitted due to **psychosis** and suicidal thoughts. Zuclopenthixol (ZC) alone, ECT combined with thioridazine (TR) and ZC, and fluoxetine (FX) combined with Li produced. . .

L22 ANSWER 4 OF 5 JICST-EPlus COPYRIGHT 2003 JST on STN

ACCESSION NUMBER: 960607740 JICST-EPlus

TITLE: Endocrinological treatment for **refractory depression**, manic-depressive illness, schizoaffective disorder and residual state of acute **psychosis**.

AUTHOR: KITAYAMA ISAO; HAMANAKA KENJI; INUI KOJI; MOTOMURA HIDEFUMI; NOMURA JUN'ICHI
KAWAKITA MASAHIKO

CORPORATE SOURCE: Mie Univ., Sch. of Med.

SOURCE: Miekenkoseinogyokyodokumiairengokai Suzukachuosogobyoin
Kansho Shogai no Shinkei Kagakuteki Seiin oyobi Chiryo ni
kansuru Kenkyu. Heisei 7 Nendo Kenkyu Hokokusho
(Neuroscientific Research on Pathogenesis and Treatment of
Affective Disorders), (1996) pp. 93-95. Journal Code:
N19961642 (Tbl. 2, Ref. 2)

PUB. COUNTRY: Japan

DOCUMENT TYPE: Journal; Article

LANGUAGE: Japanese

STATUS: New

TI Endocrinological treatment for **refractory depression**, manic-depressive illness, schizoaffective disorder and residual state of acute **psychosis**.

L22 ANSWER 5 OF 5 DRUGU COPYRIGHT 2003 THOMSON DERWENT on STN

ACCESSION NUMBER: 1987-18119 DRUGU T S

TITLE: The Use of Psychostimulants in General Psychiatry. A
Reconsideration.
AUTHOR: Chiarello R J; Cole J O
LOCATION: Belmont, Massachusetts, United States
SOURCE: Arch.Gen.Psychiatry (44, No. 3, 286-95, 1987) 1 Fig. 2 Tab.
81 Ref.

CODEN: ARGPAQ ISSN: 0003-990X
AVAIL. OF DOC.: McLean Hospital, Belmont, MA 02178, U.S.A.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature

ABEX. . . DA, and DA and MP have been successfully used as adjuvants to
tricyclic antidepressants or MAO inhibitors in patients with
refractory depression without inducing hypertensive
crises or other serious side effects. Side effects of psychostimulants
include anorexia, stereotypy, an increase in spontaneous and conditioned
motor behavior and acute paranoid **psychosis**. (E28/PMI)

=> d his

(FILE 'HOME' ENTERED AT 12:55:25 ON 11 SEP 2003)

FILE 'ADISCTI, ADISINSIGHT, ADISNEWS, BIOSIS, BIOTECHNO, CANCERLIT,
CAPLUS, CEN, DGENE, DRUGB, DRUGLAUNCH, DRUGMONOG2, DRUGNL, DRUGU, EMBAL,
EMBASE, ESBIOBASE, IFIPAT, IPA, JICST-EPLUS, KOSMET, LIFESCI, MEDICONF,
MEDLINE, NAPRALERT, NLDB, NUTRACEUT, ...' ENTERED AT 12:55:46 ON 11 SEP
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L18 129 S L16 AND L17
L19 5 S L16 (S) L17
L20 0 S L7 AND L19
L21 1 S L18 AND L7
L22 5 DUP REM L19 (0 DUPLICATES REMOVED)

=> s l19 and l8

L23 0 L19 AND L8

=> s refractory depression with dissociation

75% OF LIMIT FOR L#S REACHED

28 FILES SEARCHED...

L24 0 REFRACTORY DEPRESSION WITH DISSOCIATION

=> s refractory depression with dissocia?

28 FILES SEARCHED...

L25 0 REFRACTORY DEPRESSION WITH DISSOCIA?

=> s refractory depression

L26 1677 REFRACTORY DEPRESSION

=> s depersonalization or dissociat? or detachment or alexithymia or no feeling?

18 FILES SEARCHED...

L27 883287 DEPERSONALIZATION OR DISSOCIAT? OR DETACHMENT OR ALEXITHYMIA OR
NO FEELING?

=> s 126 and 127
L28 17 L26 AND L27

=> s 18 and 110
95% OF LIMIT FOR L#S REACHED.
L29 4049 L8 AND L10

=> s 128 and 129
MAXIMUM L# WOULD BE EXCEEDED.

=> s 128 and 129
MAXIMUM L# WOULD BE EXCEEDED.

=> d his

(FILE 'HOME' ENTERED AT 12:55:25 ON 11 SEP 2003)

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L23 0 S L19 AND L8
L24 0 S REFRACTORY DEPRESSION WITH DISSOCIATION
L25 0 S REFRACTORY DEPRESSION WITH DISSOCIA?
L26 1677 S REFRACTORY DEPRESSION
L27 883287 S DEPERSONALIZATION OR DISSOCIAT? OR DETACHMENT OR ALEXITHYMIA
L28 17 S L26 AND L27
L29 4049 S L8 AND L10